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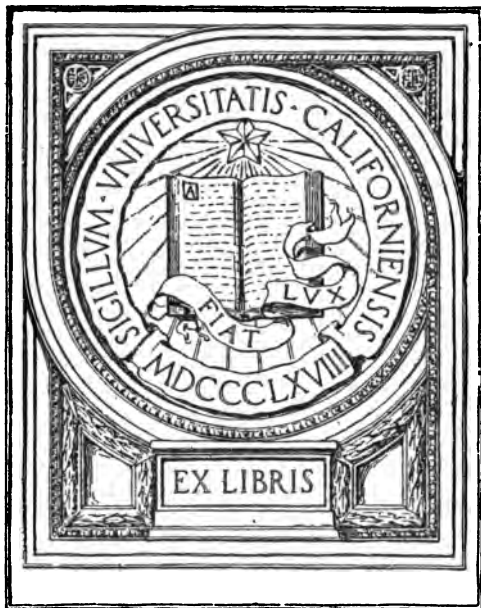
Adventures
in
Endocrinology
by

Henry R. Harrower, M.D.

2nd EDITION

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Henry R. Harrower

UNIV

**ADVENTURES
IN ENDOCRINOLOGY**

“EVERY BIBLE is first a book of revolution, and then a refuge for reaction. Yet no man can possibly know all he should know for the purposes of his own work. This fact affords the only justification for those, who cannot profess to profound knowledge in any special line, attempting to solve problems which by their nature are beyond the specialist. They may have been able to grasp in a measure the general conclusions of each science, and by a happy, perhaps accidental, combination, show at least part of the forest to those more particularly occupied with the trees themselves or the flora of the undergrowth.”—Morley Roberts in “Warfare in the Human Body.” Ch. III, p. 66. New York: E. P. Dutton Co. 1921.

ADVENTURES IN ENDOCRINOLOGY

By HENRY R. HARROWER, M. D.
Director of The Harrower Laboratory

Lots of rocks help
to make a firm
foundation.

—B. C. Forbes.

—
Second Edition
—

1922

The Literary Department of
THE HARROWER LABORATORY
Glendale, California

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by Henry R. Harrower

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TO THE
LIBRARY OF
CONGRESS

TO
my esteemed colleague
GEORGE H. SIMMONS
who, by his opposition through
twelve years, has stimulated me
more than many a well-wishing
friend

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PREFACE TO THE SECOND EDITION

THE FIRST edition having been exhausted more speedily than was anticipated, it is a pleasure to have to reprint an additional quantity. It is very evident from the scores of written and spoken comments, that this little effort of mine has aroused a lot of enthusiastic interest. Fortunately the book has first fallen into the hands of friends, and I have yet to hear from those who are on the other side. The first of the reviews comes to my attention just as the printing order is given for this second edition and I cannot refrain from passing on a few of the paragraphs from the review in the *American Journal of Clinical Medicine* (July, 1922, xxiv, p. 545) :

"This latest book of Harrower's is dedicated 'To my esteemed colleague George H. Simmons who, by his opposition through twelve years, has stimulated me more than many a well-wishing friend.' Anybody who knows Doctor Harrower personally will agree that this dedication was penned not in a sense of bravado or of sarcasm but actually in all sincerity. He, undoubtedly, has learned the truth of the statement that a man learns most from his critics.

"The little book before us is written frankly *pro domo*; that is to say, its purpose is a defense against numerous criticisms (that have appeared, notably in the *Journal of the American Medical Association* and in *Endocrinology*) of pluriglandular therapy and of Harrower's commercial activ-

ities; also a vindication of these same activities and of the views that Harrower has promulgated for years. The author does not spare his adversaries, citing passages from their polemical articles and maintaining his position. It seems to us that Doctor Harrower scores several points in this book of his, just as he has done in his earlier ones.

"After all, the physician's sole purpose and his primary duty is, to benefit his patient and to relieve him of his ailments. The establishment of a remedy or a method is only second in his interest. Nor can this be objected to; for, even in animal experimentation, there are numerous factors that tend to obscure the outcome of the experiment and, in the last instance the animal experiment is but a poor staff to lean on in establishing or in condemning any particular substance. It might be argued that it is no better than the clinical experiment. If it is as good as the clinical experiment properly conducted it is worthy of all commendation.

"Doctor Harrower's book causes us an occasional chuckle of enjoyment. The Reviewer confesses to being rather partial to the ideas that he has proclaimed for years. We, naturally, like to see him score."

It is indeed a great pleasure to send this second edition on its way, with the hope that the truth as I see it, regarding certain aspects of organotherapy and the antagonism to it by some in high places, will be made clear to those into whose hands these books may come.

H. R. H.

July 12, 1922.

ADVENTURES IN ENDOCRINOLOGY

INTRODUCTION

THE STUDY of the internal secretions, at least from my particular point of view, has proved to be quite an interesting experience. I had been working out certain ideas for some years, mentioning them occasionally to friends, wasting quite a little time and money trying to develop some notions which were not evolved from my inner consciousness, but were the legitimate offspring of the literature which I had studied, so that I might be able to use them in my practice. Before long I had developed quite an enthusiastic interest in the subject.

It was not until 1912 that I became so deeply engrossed in the study of the internal secretions that all other subjects were of lesser importance, and at that time, while in London, I began the production of the manuscript for a comprehensive book which eventually was published in 1914 by Baillière, Tindall, and Cox and called "Practical Hormone Therapy." Before the book was ready for press, I had visited eight or ten different countries and seen the majority of the men whose literary contributions suggested that they were among the most important students of the internal secretions. Personal contact in all matters pertaining to the acquirement of knowledge, can-

not possibly be overrated for it brings one cheek-by-jowl with him who has an expert's fund of the vital things one wants to know. Many of these experts later went over the manuscript for the various chapters of my book.

I enjoyed this personal contact hugely and it fanned the spark of my enthusiasm into a real blaze.

On my return to America, I engaged in literary work for a while in the East, and then came to California. During a period of comparative idleness in my new home, I wrote to a number of my friends in the hope of correlating their work in this special field, and as a result of this correspondence, had the honor of founding the Association for the Study of Internal Secretions in 1915-16.

While this was a great advance, I did not succeed in accomplishing all that I had hoped through this Association. I felt that a bulletin was necessary to bring together the interests of those studying this subject in different parts of the world, and *Endocrinology* was the result. I felt that there should be an actual, personal get-together of those especially interested and there has been an annual meeting each year since.

I spent much effort in gathering together ten sets of reprints and books on the internal secretions with the expectation that these would be filed by subjects in various medico-literary centers in this country and abroad so that members

of the Association might have convenient access to these reprints directly or by post. Many thousands of reprints have been collected but as yet I do not believe they have been made especially easy of access. Perhaps some day they will be in reach of all those who are intensively studying endocrinology.

The above were not the only ideas which were with me at that time, for there were quite a number of others, but mention of all need not be made here. Yet I would be doing myself a great injustice if I were to overlook one that appealed to me greatly and which in fact later took precedence of all the others—the establishment of an institution with facilities for developing the various ideas in this field that seemed likely to be practically helpful, but were difficult of materialization. In short, I wanted to make it possible for physicians other than those who “specialized” in endocrinology, to derive a degree of clinical knowledge from the things that were being expounded in the current literature so that they would be brought closer to all that was of interest in the study of endocrinology.

When I realized the impossibility of establishing a department in connection with some large teaching or research institution and how problematic it was to influence any wealthy persons to finance it, I took the matter altogether in my own hands with the result that what is known as The Harrower Laboratory was established. This laboratory has

called forth praise in certain quarters and adverse criticism in others. In this respect its career has not been unlike the careers of other institutions. The fundamental idea of this laboratory is service to the profession—a specialized service to “materialize ideas pertaining to the internal secretions in general practice.”

Some years ago, by reading of the splendid clinical work of Henri Claude and his pupil Gougerot, of Paris, as well as many subsequent papers on various aspects of the subject, I got hold of THE PLURIGLANDULAR IDEA which sounded very good to me and when I investigated it for myself I found that it contained some real gold, though even in these days, one critic calls it “fool’s gold.” I began to pan for more and have much that can only be considered the real thing. I have been scorned for seeking gold in a locality in which its presence was denied; I have been derided for attempting to pan for it in an unaccepted fashion, and I have been taken to task by my critics for expressing myself in terms and through media that were unorthodox.

The commercialism—that much abused term which like the poor is with us always, though we are ashamed to confess that all of us are more or less “afflicted” with it—which was a necessary part of the work of my laboratory, sent cold chills down the backs of several of my colleagues in the Association for the Study of Internal Secretions, and a few of them have attempted in an

aggressive manner to show the errors of my ways in no mistakable terms.

As was to be expected, and in the natural sequence of things as they obtain today in these United States, it was not long before the arbiters of therapeutic "morals"—The Council on Pharmacy and Chemistry of the American Medical Association—had singled me out for a special attack on the score that many of the glandular remedies I used and recommended were not in the United States Pharmacopoeia or the "N. N. R.", hence were not recognized as effective remedies. This meant that any of my formulas containing these tabooed products could not be accepted by "The Powers That Be." But the criticism did not stop here, for what was most reprehensible about my formulas was that the idea of combining glandular extracts was a reversion to the old-time polypharmacy.

I answered their first criticism by saying that no remedy ever could attain a place in the U. S. P. or "N. N. R." until it had been shown to be clinically useful. This could only be found out by using it. Hence somebody has to be using non-official products, else progress must stop entirely. Their second comment I denied point blank as entirely contrary both to experience and to logic.

Since then I have consistently held to the fundamental physiological principle that *the glands of internal secretion are related*, that disturbances in one of them necessarily must be reflected in the

functions of the others which are related to them, and that pluriglandular therapy needs must be a more reasonable procedure than the use of single gland extracts.

The more I think of the attacks that have been made on my work the more philosophical I am, and though in the beginning my resentment was intense, perhaps too intense, I am so sure now that I am in the right and that those who are opposed to me are wrong that whether I am correct or not must be left to my readers. My object in writing this book is merely to collate some of the attacks which have been made on me and prove to what lengths narrow prejudice will drive man. In short, I expect to present here facts from which the reader may draw his own conclusions, and it is my hope that he will draw his own conclusions unbiased by what he has heard or read about me. In this book I am going to stand before the medical profession unashamed and unabashed, and I am not going to throw down the glove for a fray. I am through with war and want peace—peace with honor, the only sort of peace that is worth while. I have no doubt that my opponents are men of worth and I have no doubt that in their opposition they thought they were helping the cause of “clean” medicine.

Let me emphasize here that the mood that is upon me as I pen these lines is one of peace to my colleagues—without rancor, without malice. But let me also emphasize here that I am not in the

least contrite nor regretful for what I have done in the past, nor have I any misgivings as to my future course which will be along the same lines as in the past, with this difference only, that a greater development will be my object. Whether among my harsh critics have figured the editor of *The Journal of the American Medical Association* and other editors, or certain physiologists and physicians in high places, I have only the kindest thoughts for them—thoughts which all right-minded men have for their opponents.

Since fallibility is a distinctly human attribute, I can not very well say that none can controvert my statements. Rather will I say that I have had every reason to believe that I have been and am still right fundamentally, and have always attempted to pass my judgment with as many as possible of the facts before me. I shall be very glad if any reader who may be interested, and has any additional facts to submit, will give me proof either unpublished, or with the reference, to disprove my attitude as it will be outlined in the following chapters.

Another matter that may be mentioned is illustrative of a trait in human nature that has been known to all from time immemorial. When some of my opponents are asked if they have ever used any of Harrower's products, they invariably throw up their hands and assure their questioners that they would "never think of using such stuff." This "gesture" on the part of my opponents would

be acceptable to me if they had had clinical experience with my remedies; but when they have not had any experience, which is invariably the case, their attitude is far from commendatory. How in all reason can one insist that a man is fundamentally wrong, and decry the results of his work if one has withheld himself through prejudice from the slightest use of his suggestions, and go even a step further and deny the statements made by those who are in a position to give a just opinion because of a full knowledge based on the indisputable fact that the ideas have been used and have not been found wanting?

To illustrate this strange vagary of human nature I shall cite a conversation between a friend of mine and a certain Baltimore physician who betrayed the involved workings of his mentality in the following remarkable manner:

"Pluriglandular therapy is no good. There are only a few glands that are any good. Harrower has done more against organotherapy than any other man in the country and I really think he has made a fool of himself. He makes too many claims. Why—he doesn't know anything about organotherapy anyhow. . . . Of course it is easy enough to get statements from crossroads doctors to the effect that they have gotten wonderful results with this and that that Harrower sells, but it doesn't mean anything. . . . Unfortunately, Harrower came out with his sales work

just as the profession was beginning to realize the value of the glands, notably the thyroid. . . ."

I must demean myself, disagreeable as it is to me, to deny categorically several of these remarks. First, "Pluriglandular therapy is no good." This statement in itself is tinged with asininity since the contrary long since has been proved. Secondly, as for Harrower being a fool, would it be immodest in me to deny so distinguished an allegation?

Again, "the crossroads doctor" is indeed a despicable character—he knows naught of truth—how can he? And is easily led astray, hence he represents ignorance in the medical profession—in the minds of some who think well of themselves! Our medical Main Streets are peopled with quacks and only in cities of a million or more do education and truth abide.

And, fourth, *Harrower did not come out with his sales work "just as the profession was beginning to realize the value of glands, notably the thyroid."* The beginnings of thyroid therapy are thirty years old and the development of my laboratory has taken place in the four years since the beginning of 1918, and I am willing to believe what I have been told many times, that I have had some part in arousing medical opinion in regard to the importance of the routine study of the endocrine glands, and, especially, the value of pluriglandular therapy.

In passing, it is interesting to note that my correspondent who was good enough to send this report to me, remarks rather sagely: "I note with much interest that these fellows who have so much criticism and advice to hand out against your work have not used your products, and generally are the ones whose waiting rooms are empty. The physician who has up to a dozen patients waiting for his services, invariably is ready to do anything to produce results, for he is the man who is carrying the load of sick folks."

With the above in mind, it certainly is strange how uniformly the kicker has to admit, usually somewhat shamefacedly, that he has had no personal experience, whereas the booster says, "Sure, I have been following this thing for three years and would be convinced out of my own personal experience without hearing a word from any source"—or words to that effect.

It is also a strange thing that every principle of any magnitude, any doctrine different in the slightest degree from the orthodox, any invention that is entirely original, has got to go through the stage of derision by somebody.

Nothing important that has been done in this world has been free from attack of some sort and the work that has been developed out here in The Harrower Laboratory in Glendale, California, certainly has run true to form and has been subjected to considerable criticism. Despite this fact, however, it has established itself throughout the

United States and in a number of foreign countries as a worth-while addition to those factors furthering progress in medicine, and its phenomenal growth in four short years is tangible evidence of the esteem with which its work and products are held by some.

This book, written in the stress of battle for what I firmly believe to be a fundamentally correct and reasonable principle, is an attempt to direct attention both to the criticisms and to the answers to these criticisms.

As to what the verdict about my position will be must be left for the reader to decide, and it is very fortunate that there is plenty of opportunity to verify the decision in an individual manner, for after all, the medical profession at large must be the final court of appeal.

I

THE DEVELOPMENT OF "PSEUDOENDOCRINOLOGY"

"Things true and evident of necessity must be recognized by those who would contradict them."—Epictetus.

"PSEUDOENDOCRINOLOGY" is a term that was born in 1921. Evidently it is a child of the brain of R. G. Hoskins, at one time Professor of Physiology at the Northwestern University and more recently occupying the same chair in the Ohio State University, Columbus, Ohio. Pseudoendocrinology, as its name indicates, is this writer's conception of an endocrinology which is imaginary or supposed. One of the first statements embodying this term is the editorial by Hoskins entitled "What is Endocrinology?" in *Endocrinology*, September, 1921, v, p. 610.

"There is a class of writers who affect the term 'so-called endocrinology,' the implication seeming to be either that the existence of endocrine organs is doubtful or else that the voluminous literature pertaining to them is of such uncertain significance as not to deserve formal recognition. That the literature does include an intolerable deal of twaddle, no well-informed reader can deny. Such pretentious nonsense might well be designated *pseudoendocrinology*."

It may be interesting to recall a little history regarding my relation with Prof. Hoskins. Early

in the formative stage of the Association for the Study of Internal Secretions in 1916, I visited him at the Northwestern University on South Dearborn Street, Chicago, and aroused a lively interest on his part in what work had been projected for this embryo organization. As a result of this visit Hoskins' interest was sufficiently aroused to make him accept a position on the editorial staff of a projected periodical which has since developed into the position of Editor-in-chief of *Endocrinology*; the Bulletin of the Association for the Study of Internal Secretions.

I have had many friendly letters and evidences of Hoskins' personal interest in my work and the work of the Association in which we are mutually interested, but as The Harrower Laboratory developed, and its promotion department brought its work before the medical profession in a business way, there developed in Prof. Hoskins the feeling that he must stand up for what he called purity in endocrinology, as against my "pretentious nonsense" that he has called pseudoendocrinology. Each of us is attempting to add his little bit of service to humanity. Hoskins, still a physiologist, though he graduated as a physician at Johns Hopkins University last year (1921) sees things largely as a physiologist, while I, on the other hand, am the same aggressively interested ordinary doctor that I was when I first had the pleasure of meeting this gentleman who now seems to be arrayed against me.

Hoskins, from his editorial chair, feels that the study of the internal secretions is being besmirched by me because of my erring viewpoint, whereas I, on the other hand, feel that I have a right to look at things from a little different angle than Hoskins and, consequently, to disagree with him.

I can't help but think that Hoskins and some of his colleagues are afflicted with the disease known as misokainia, and therefore should be commiserated with rather than laid open to criticism. This word misokainia (*miso*—hatred; *kainos*—new) was originated by the late Achilles Rose of New York, as a substitute for the philologically incorrect word "misoneismus," which Lombroso applied to the deep-rooted tendency of mankind to combat new ideas and discoveries—one of the great bars to human progress. Rose pointed out that "this hatred of the new may become a phrenitis—a distinct type of mania—when the misokainist may resort to contemptible weapons such as deliberate misrepresentation and interference and, perhaps, even personal animosity and attack."

The development of pseudoendocrinology, with its sanguine viewpoint, is believed to be "exerting an influence detrimental to further progress," as Hoskins puts it, although in almost the next breath he makes the statement that

"The overenthusiastic class exerts an unfortunate influence largely by giving point to the strictures

of the first mentioned group. [Those who refuse to believe at all.—H. R. H.] In the long run their very extravagance will serve as its own antidote, but as a passing phenomenon their confident exploitation of systematized delusions is awakening false hope in the minds both of patients and of physicians."

The above statement, appearing early in an address by Hoskins entitled "Some Current Trends in Endocrinology," read before the Columbus Academy of Medicine and published as the leading article in *The Journal of the American Medical Association*, November 5, 1921, lxxvii, p. 1459, is but one of many hints that the current trend apparently is in the direction of what is called "pseudoendocrinology" and is to the detriment of medicine as a whole. It is possible that Hoskins is right and in his position he is joined by a number of other individuals, but it is also equally possible that the opposite may be true, and it is quite interesting to note that another statement in the same article reads as follows:

"The overenthusiastic group offer in justification of their imaginative daring and therapeutic rashness the plea that it is only by extensive experience that we can hope to learn either the possibilities or the limitations of endocrinology as a branch of practical medicine. In this they are, of course, occupying an impregnable position. . . . Recklessly administering endocrine products to all sorts and conditions of patients, happily claiming as therapeutic triumphs

all changes for the better and ignoring failures, is not likely to result in any very substantial progress."

The above quotations rather smoothly indicate that certain procedures recommended by me (because I have found them frequently recommended by others and after having tried them myself I found them good and was willing to pass them on) are "imaginative," and when applied are evidences of "therapeutic rashness." But it is good to know that Hoskins has to admit that I, with those who agree with me in regard to empiricism—a matter to which I have given some consideration in a future chapter of this book—are "of course, *occupying an impregnable position.*" And I feel quite confident that the position is indeed impregnable; and that we never can be ousted from it.

It will be seen in the pages which follow that a very decided assault is being made upon this impregnable position and I purpose to defend myself in it as best I can.

Another statement in Hoskins' paper may be quoted:

"Any number of absurdities have appeared, are appearing and will appear because men so readily believe that which they wish to believe. There is only one way to circumvent the *post hoc* fallacy, and that is to maintain adequate and rigid controls. . . . Reports of cures are convincing only when accompanied by adequate evidence that suggestion and other accessory therapeutic

measures, as well as mere coincidence, have been ruled out as the determining factors. . . . So long as practitioners fail to realize the essential requirements of scientific evidence and to educate their patients along this line, not only pseudoendocrinology but also a multitude of other pseudoscientific cults will continue to flourish."

I have given a good deal more consideration to the subject of suitable controls in Chapter X, "Properly Supervised Controls", and in passing merely wish to say that the most convincing "adequate evidence" that we can have as to the value of a procedure and the correctness of the one who recommends it, *is the patient and his changed clinical situation*. I have admitted repeatedly in my lectures and publications that it is entirely impossible to know just exactly where the value of an organotherapeutic procedure begins and where it ends, and my interest in the subject has not permitted me to become so engrossed in this one corner of medicine, that matters which necessarily must be considered simultaneously are ignored.

In other words, my conscience will not allow me, when confronted with a problem which may be solved by the application of some principle of "pseudoendocrinology" to limit my recommendations to the organotherapy alone. (A little hint which extends this viewpoint will be found in my reference to the lecture by Dr. John L. Tierney, of St. Louis, at the California State Medical Society

held last May (1921) and considered more fully in Chapter X. Every obviously needed measure should be added to it. It would be manifestly unfair, and, in fact, it would clearly constitute malpractice if, when confronted with a complicated problem, a physician would ignore every contributory factor and treat the most obvious condition alone.

My chief point in establishing my position, which Hoskins admits is impregnable, has been my insistence that the endocrine aspects of the routine problems of general practice have been ignored persistently by the medical profession, and in directing attention to them and urging measures calculated to modify them, I believe that I have broadened the viewpoint of many a doctor and also made possible results that had not been attained previously.

I grant that my critics can say that if Harrower insists upon detoxication and remineralization and dietetic control and the removal of foci of infection and the regulation of the fundamentals, that any or all of these measures may be the ones chiefly responsible for any therapeutic progress in a given case; but it must not be overlooked, in this connection, that the same reasoning must apply to the use of any other therapeutic procedure. It is also a fact that the majority of the cases that have been treated at my suggestion, and in whose treatment the profession has been interested in applying pluriglandular therapy, already have

been "through the mill," and perhaps may have perambulated from one physician's office to another for months or even years.

A far greater difficulty which I have had to encounter in my work, than the opposition of the scientists, has been the very natural attitude on the part of the general practitioner to apply my recommendations when he knows nothing better to do—in other words, when he is "at the end of his rope" and does not know which way to turn—and in spite of this really tremendous handicap we have made our mark. This indicates to me that the application of the pluriglandular idea, even late in the day and when many other measures had failed, justifies its recommendation and the principles upon which it has been based.

Here is an opportune comparison: We say that "America really won the World War." Yet if such a claim is made before a Britisher or a Frenchman, the Britisher very properly will immediately say, "What would have happened if there had been no British navy?" and the Frenchman, equally right, will say, "What would have happened if our boys had not said at Verdun, '*Ils ne passeront pas du tout,*' and given life to their words by their deaths?"

I think this is a very excellent simile. The French made their efforts, succeeded occasionally and failed almost as often. The Canadians at Vimy Ridge made their advances, but had to take their reverses. The British in their sectors, the

Portuguese in theirs, and in fact, every army involved, from Flanders south, made their temporary gains and lost them for four long years. Then a new factor was injected, a new alignment took place, and everybody said, "Let us, with one accord and as one great whole, get together and go out to win." They did it, and they won, but not until they worked TOGETHER. And this is exactly the way that I see it in so many cases.

Advances are made by the application of some accepted measure; reverses come by overlooking a weak point or allied condition. Still further advances may be made in the hands of some other doctor by applying some other measure, and it is only when a new alignment takes place, the patient is considered as a whole, *the vital endocrine aspects with the rest*, and an altogether concerted effort made, that the "war" is ended.

What do we care whether the Americans won the war? Or the French? Or the British? Or to put it very frankly, what do I care whether the results are solely due to the advised organotherapy or to the *tout ensemble* of the treatment? I could not ignore the other sectors and fight on the organotherapeutic line alone, and apparently in many an instance the best directed efforts upon all the other sectors have failed until the broader and more comprehensive view has been taken.

This may or may not offset Hoskins' statement: "Reports of cures are convincing only when accompanied by adequate evidence that suggestion

and other accessory therapeutic measures, as well as mere coincidence, have been ruled out as the determining factors."

Nevertheless, I shall make the utmost use of suggestion and recommend it when called for. It would be altogether wrong to ignore the "accessory therapeutic measures" in order that we might see how effective our organotherapy might be alone, and despite the fact that this may obscure a decision as to which factor was the decisive one, or in what degree various measures were valuable, the interests of the patient come first, and I shall continue to advise the "pseudoendocrinology" which some insist on criticizing.

Further on in Hoskins' address he emphasizes the facts that "endocrine physiology is largely in a state of uncertainty" and also that "deductive reasoning can be productive only when the premises are sound." His methods of judging premises do not seem to harmonize with those of others, and he follows the above statements by the following:

"A few examples of more or less dubious premises in current vogue may be cited. We are glibly told of the 'complex hormonal equilibrium' of the blood. However probable the existence of numerous circulating hormones, proof of their existence is almost completely lacking. . . . Much is made by some writers of 'hormonic antagonists.' . . . In short, the existence of hormonal antagonism remains yet to be proved, however fascinating it is to theorize about."

Presumably acceptable proof in the eyes of this critic will consist in being able to analyze the blood and isolate from it the varied and almost innumerable substances which we presume are circulating therein. This is, of course, hoping too much. It is passing strange that a man who has done so much experimental work with internal secretions should at this late stage question the existence of the hormones and confirm his position by the statement that "proof of their existence is almost completely lacking."

There is no proof of the presence of amboceptors and receptors, as predicated in the "side chain theory" of Ehrlich, who apparently has explained to the entire satisfaction of both the technical as well as the practical members of the guild, the philosophy of the immunizing response of the body and how the body disposes of toxins by the production of antitoxins, and so on. One might equally say, referring to these antibacterial and antitoxic factors that "proof of their existence is almost completely lacking"—in fact, it is *entirely* lacking, for they are figments of Ehrlich's imagination.

Whether Hoskins believes in a "complex hormonal equilibrium"—a term which he happens to be quoting from one of my articles—or not, cannot dispose of the reality of this equilibrium, nor can it lessen its complexity; and insofar as normal antagonists are concerned, no less an authority than Sir Edward A. Schafer, Professor of

Physiology in the University of Edinburgh, insists that the term "hormone," representing the activating principles of certain organs, is a misnomer because not all the internal secretions activate. Some of them have an entirely opposite effect. In fact, they are, as Professor E. Gley, of Paris, has called them, "antihormones" or as Sir Edward himself calls them, "chalones," from the Greek word meaning to relax—those whose action is of an antagonistic nature or inhibitory.

Then Hoskins refers very gently to my hypothesis of hormone hunger in the following terms:

"A fantastic theory that has had some currency is that the body cells have a capacity to select from a pluriglandular mixture any hormones they happen to need and to discard the rest. All the evidence is to the contrary. Both clinically and experimentally it is sufficiently plain that the law of mass action has not yet been repealed. If the blood is flooded with thyroid substance, for example, the subject dies of thyroid intoxication quite as would be expected. Many other guesses, masquerading as facts, could be cited, but let these suffice."

And this particular subject is so interesting that it will be given consideration in an "Adventure" all by itself! See Chapter V, "Harrower's Hypothesis and Hoskins' Hallucinations."

Whether my endocrinology is of the "pseudo" variety or not, the reader undoubtedly will find in the following pages that I have not merely the courage of my convictions but the added weight

of the published statements of many an authority whose position has been established as a result of years of clinical study and has been repeated in the literature times without number.

I would rather be a pseudoendocrinologist out in the battle front, fighting to acquire better control over disease than to be ever so scientific an endocrinologist who stays at home and criticizes the methods whereby we accomplish our advances.

As the deathless Thomas Huxley once said, "Sit down before a fact like a little child; be prepared to give up every preconceived notion; follow it wherever and to whatever abysses it may lead you—or you shall learn nothing." Or as his equally famous contemporary Thomas Carlyle said, "Surround truth with bitter denial and contradiction and you furnish it with the soil for its permanent growth."

II

HYPOADRENIA—

“THE FOURTH DIMENSION IN MEDICINE”

“Facts remain such, despite denial, and no amount of opposition can change the character of truth.”

IN the May, 1921, issue of *Endocrinology* is a paper by Professor George N. Stewart, of the Western Reserve University, Cleveland, Ohio, entitled, “Adrenal Insufficiency.” This article consists of a resume (14 pages) of the physiological data developed in the past few years, and “Some Clinical Views” (6 pages) which are of very unusual interest to me.

Considerable study is given to the literature regarding the influence of the removal of the adrenal glands, as well as to references to measures calculated to interfere experimentally with the function of these organs in dogs. Naturally, Stewart emphasizes the position taken by himself and Rogoff in the experimental work which he believes has disproved some of the conclusions made several years previously by Prof. W. B. Cannon, of Harvard University, in regard to the influence of emotional factors upon adrenal functioning, but his opposing position has not been as generally accepted as has that of Cannon, although some of his remarks may be considered as well taken.

Stewart believes that the experimental evidence has tended more and more to show that the cortex

is "the part of the adrenal indispensable for life. It is the cortical tissue which alone, or at any rate most conspicuously undergoes compensatory hyperplasia, when a deficiency is created by removal of a considerable part of the adrenal tissue."

This, of course, undoubtedly is true and probably explains the therapeutic advantage of total adrenal substance over the medullary principle, adrenalin, when used in the conditions which are termed by so many clinicians "adrenal insufficiency." It is also explainable by the histologist's claim that approximately 85 per cent of adrenal tissue is cortex, as compared with only 15 per cent of the chromaffin cells or medulla.

With this in view, Stewart properly remarks:

"It is a curious thing that while the great bulk of the experimental evidence emphasizes the importance of the cortex . . . the bulk of clinical writers seem almost to ignore the existence of the cortex. 'Adrenal insufficiency' in nine clinical papers out of ten . . . seems to connote interference with the output of epinephrin and consequent derangement of functions in which epinephrin is assumed to play a leading rôle. . . . It is very common indeed to find the conclusion drawn that because the epinephrin store was found smaller than the average, perhaps many hours after death, the 'adrenal function' must have been depressed and the patient must have suffered from adrenal insufficiency during life."

Stewart, apparently pleased to find one writer who partly agrees with him (René Porak:

L'hypertrophie et la teneur en adrénaline des surrénales dans les infections, les intoxications et certains états d'immunité. *J. de Physiol. et path. gen.*, Paris, Jan. 1919, xviii, p. 95) refers to Porak's experiments in the Municipal Laboratory at Paris, as follows:

"He remarks apropos of the innumerable researches on the condition of the adrenals in infections and intoxications prior to his own work, that the existence of the same histological changes in the adrenals in infection and in immunity prove in a definite fashion the excesses of the theory of adrenal insufficiency in infections and intoxications. It is as welcome as it is unfortunately rare at the moment, to find in the French clinical and pathological literature a protest against the fetish of adrenal insufficiency. Gley and his co-workers have given but a cool reception to the complementary doctrine of what may be almost termed 'adrenal all-sufficiency' in physiology."

Then concluding his comprehensive consideration of the large amount of experimental data on this subject, Stewart says:

"On the whole, then, it must be granted that hitherto the attempts made to evoke in animals a well marked syndrome characteristic of adrenal deficiency, have been singularly disappointing. The contrast is great when we leave this desert, where the physiologists and experimental pathologists have wandered, striking many rocks but finding few springs, and pass into the exuberant land of clinical endocrinology, flowing with blandest milk and honey almost suspiciously sweet."

These conclusions are not very encouraging, and I shall have something more to say about this last insinuating phrase a little later.

Just because it is not easy for the laboratory worker to reproduce the syndrome of adrenal insufficiency in dogs and because the results of many tedious experiments reported "have been singularly disappointing", is no proof to a clinician that such a condition cannot exist in human beings. One can produce diabetes mellitus in dogs by removing the pancreas in the accepted three-step fashion; one can also produce colitis in animals with great ease by introducing irritating substances in the bowel; and it is possible to produce many other conditions in various animals in order to study them and to develop means of controlling them through animal experimentation, but according to Stewart it is not easy to produce adrenal insufficiency. Either the dog is killed as a result of the ablation of the glands or the healthy out-of-doors animal overcomes the less drastic conditions too quickly to permit of the development of a "well marked syndrome characteristic of adrenal deficiency."

Without belittling the laboratory, for endocrinology owes much to the painstaking efforts of the laboratory workers, we must not allow ourselves to arrive at conclusions such as Stewart advises merely because he cannot reproduce in animals certain clinical symptoms which happen to be un-

usually common in human beings under certain quite usual circumstances which are encountered almost every day in the routine of general practice.

In his much more brief consideration in his paper of the clinical aspects of hypoadrenia several points are worthy of mention. For example, he refers thus to the work of Claude and Gougerot, who, by the way, were among the first to emphasize the importance of pluriglandular syndromes, (they) "put forward in 1908 what they considered as a new conception, that certain complex symptoms are due to primary insufficiency of more than one of the endocrine glands. There is no reason in the world why this should not be true." And in this, at least, I thoroughly agree, for it happens that this admission by Stewart is true.

Again, it is surely not necessary when there is a disturbance of endocrine function that it should be manifest histologically or pathologically at autopsy? Functional disorders need not cause organic changes. It should not be forgotten that a large part of the deductions of a physiologist, based upon animal experimentation, depends upon the histologic study of the tissues supposed to be influenced, whereas, as regards our clinical experiences, we are concerned with changes which do not necessarily have to reach a structural degree, nor is the opportunity presented to see such changes either with the naked eye or by the aid of the microscope.

Pause should be made here to mention an expe-

rience I had in Indianapolis. Sometime ago my friend, Doctor Samuel Earp, hearing that I was in Indianapolis, invited a number of his friends to meet me at the Marion Club, where we had a round-table discussion on the internal secretions. When I was in the middle of a consideration of my favorite topic—adrenal insufficiency—Doctor Earp interjected the suggestion that one of his colleagues then present, Doctor Edwin Kime, might make some remarks which would be particularly apropos under the circumstances. I had just been emphasizing the importance of adrenal depletion in toxic conditions, especially influenza, and Doctor Kime made a statement substantially as follows:

“You may be interested to know of an opportunity I had while in the service to do some autopsy work on over 150 soldiers, all of whom had died of influenza. In our study of the pathological anatomy of the adrenal glands we found that in quite a generous percentage of cases there were macroscopic changes in the adrenals, whereas upon microscopic study practically every case showed divergencies from the normal.”

In view of the very large number of cases that it was possible to bring to autopsy at Camp Zachary Taylor, and the thorough work done by Kime in conjunction with his associates Lucke and Wight (see their paper: “Pathological Anatomy and Bacteriology of Influenza,” *Arch. Int. Med.*, Aug. 1919, xxiv. 154), a report of this kind nat-

urally was a source of very considerable encouragement to me, and in the years that have passed no opportunity has been found which could add more emphasis to what Doctor Kime told us that night. There is, however, a small monograph in Portuguese, written in 1919 by da Fonseca of Rio de Janeiro, entitled "Da Insufficiencia Suprarenal na Grippe", to which I will refer here. Da Fonseca cites a number of autopsy findings indicating that changes in the adrenal structures were not infrequent in patients who had died of grippe. These included microscopical and, occasionally, macroscopical phenomena of congestion, especially in the cortex; and at times inflammatory and edematous manifestations were present with leucocytic infiltration, slight hemorrhages and even foci of necrosis.

This Brazilian writer urges the importance of the adrenal aspects of influenza; and insists that hypoadrenia almost invariably is present and that it is of decided importance as a fatal complicating factor. He emphasizes that the adrenal aspects of influenza deserve to be studied *and treated* in the less serious cases, and many experiences in hospital and private practice in Rio de Janeiro have convinced him that organotherapy opposed to hypoadrenia is a sound therapeutic measure. Quoting from this writer we find that he states: "of the reality of influenzal hypoadrenia, modern clinicians are fully convinced, for in the recent (1918) pandemic which attacked humanity as a

whole and to which Rio de Janeiro paid such a heavy tribute, the profession was once again made aware of its importance."

And later, after referring to the paucity of information on the subject, in American and European medical reviews, he quotes Prof. Ricaldoni of Montevideo, Uruguay, who asserts positively that

"this adrenal insufficiency is inseparable from influenza itself" and who further affirms that "the adrenal insufficiency of influenza accordingly is more fundamentally significant than that which may appear in all or nearly all of the general infections and many forms of intoxications."

To return to Stewart's article: Reference is made to many of the articles by various writers, chiefly abroad. For example: Nicola Pende, of Palermo, is stated by Stewart to speak "of the hypoadrenal constitution as a clinical and pathological entity first studied in Italy (constitutional angiohypotony of Ferranini)"; and then he continues:

"In reading this paper and many others by 'clinical endocrinologists,' especially the French and the Italians, the physiologist can scarcely escape the feeling that here he has broken through into an uncanny fourth dimension of medicine, where the familiar canons and methods of scientific criticism are become foolishness, where fact and hypothesis are habitually confounded, and 'nothing is, but what is not'."

Stewart then refers to the work of Eppinger and Hess of Vienna, with sympatheticotonia and vagotonia, to references by several French writers to a group of cardiopathies in soldiers which are sometimes called the "hypoadrenal types of Satre," and also to references to the neuropsychic origin of certain adrenal insufficiencies, and then arbitrarily concludes that "there is no evidence of 'adrenal insufficiency' in these patients which will stand the test of critical examination for a moment."

The most interesting work done by Prof. Josué of Paris on adrenal asystole does not come in for much favorable consideration. Stewart says that this "is the name given to a supposed syndrome in which sudden death from heart failure is apt to occur, associated with the presence of disease or marked diminution in size of the adrenals." And, by the way, it really seems as though Josué's work was backed up very thoroughly by a large clinical experience, verified by numerous colleagues, and still further verified by a good deal of post-mortem work; and yet, somehow or other, Stewart cannot see it, for he decisively ends the matter by saying:

"There is no real foundation for the view that the heart stops because the adrenals naturally supply a physiological stimulus necessary for its contractions. But it is very probable that if the adrenals are extremely diseased, the profound changes in the metabolism which must be pre-

sumed to occur will affect the heart, as well as other organs."

From my own comparatively limited clinical experience, I really believe that this is exactly what does happen though the changes are not limited to conditions related to "extremely diseased" adrenals. The serious outcome of the addisonian syndrome is both direct in its influence upon the cardio-vascular mechanism and indirect in its influence upon the other endocrines and the metabolism which it is well known that they regulate. We must not forget that Stewart already has, admitted elsewhere in this same article that "profound changes in metabolism" are caused by the experimental ablation of the adrenals, and in order to come to this conclusion, surely he must have proved these changes to exist beyond the possibility of doubt, since he uses the phrase so confidently.

Now, comes one of the most remarkable of all of Stewart's statements. Immediately following the discussion of Josué's presumed misapprehensions, he refers to a syndrome of hypoadrenia that has been described in soldiers suffering from infectious icterus in Italy by certain writers, including Frugoni and Gardegghi; also to a similar adrenal syndrome that Frugoni has connected with typhoid fever; and that several French writers, including Rivière, Fillerval and others, connect with the toxic alimentary dysenteries; as well as an adrenal insufficiency believed to accompany va-

rious indefinite infections by Carles and Satre of Bordeaux, and then, *mirabile dictu!* Stewart says the opinions of these men "can scarcely be more at present than the product of an undisciplined imagination!"

I have never tired of re-reading the above quotation, for it always brings home to me the thought that Dr. Stewart has small regard for clinicians, especially Italian clinicians. No small wonder, indeed, it must be to all intelligent physicians who know anything of Italian medicine to read the above "inspired" lines which indicate beyond dispute that Stewart classes the Italian clinician with the usual "dago" one meets in this country—the man who never rises above the lowly state into which fate and lack of opportunity have thrust him. That there is a difference between an Italian street laborer and an Italian physician need not be expatiated on here; the facts are too evident.

Not belonging to the class of "intelligent" critics to which Stewart just referred, I am "weak" enough to believe that these Italian writers are men of probity and also of acumen and that their statements are the result of powers of observation which are not despicable.

As if Stewart's low opinion of those mentioned in the quotation were not enough, he follows this up with a fling at Sergent of Paris, a man who, in my opinion, is at the head of all who have developed a clinical knowledge in this line and whose book "*Etudes Cliniques Sur l'Insuffisance Sur-*

rénale" is indisputably of so high a quality that he must be purblind who is not won over by his exposition of adrenal insufficiency. But Stewart is among those who are obdurate—perhaps the most obdurate, for his bull of excommunication reads thus:

"There is no experimental evidence whatever that fatigue diminishes the output of epinephrin, and of course, no evidence that the function of the adrenal cortex, whatever it may be, is diminished in that condition. Until we have such evidence, what is the use of a clinical observer looking at a sick man and saying 'No doubt he is suffering from capsular exhaustion due to excessive war fatigue,' or to so-called shell shock (Carles)?"

The above quotation is fortified by a jocular simile to the effect that since there have been certain clinical reports of pharmacodynamic or therapeutic effects from adrenal therapy "Hoskins [a clinician of less than a year's standing—H. R. H.], for instance, asks very pointedly whether because cascara is efficacious in relieving constipation we ought to conclude that this is because the patient is suffering from hypocascarium?"

Can it be gainsaid by any fair-minded person, after reading the above quotations, that the statements emanating from Hoskins and Stewart have not a puerility and inanity which condemn them at first blush?

Emile Sergent, of Paris, whose pioneer work

has been a large factor in initiating and maintaining my interest in hypoadrenia and whose writings were among those criticized by Stewart, made reference to his article in a communication published last October ("L'Insuffisance surrénale devant les récentes critiques des physiologistes", *La Presse Médicale*, Oct. 12, 1921, xxix, p. 813), and his very kindly worded criticism of Stewart is subjoined:

"Acquisitions derived from clinical observation cannot be regarded as non-existent. I may be permitted, in this connection, to raise my voice against the somewhat excessive criticisms made by Stewart in his recent article (loc. cit.). I think that the best and most courteous rejoinder which I can make to this eminent physiologist is that he does not know French sufficiently well to have thoroughly grasped the thought of the French clinicians. By way of proving this statement I have ascertained that he attributes to us, quite gratuitously, the view that adrenal insufficiency is insufficiency of the secretion of adrenalin. This was never our thought, and by way of assurance on this point I will state, once again, that, with L. Bernard, I described the syndrome of acute adrenal insufficiency in 1899 and that adrenalin was discovered in 1901, *two years later*.

"Moreover, recently I had the privilege of chatting with Prof. E. Gley upon this question which interests us both so vitally, for varying reasons, and I had the satisfaction of ascertaining that he shared my view. I was too well acquainted with his scientific mind to doubt for one moment that he attached no value to facts rigorously observed by clinicians."

I fear, however, that Stewart's knowledge of French is better than Sergent gives him credit for, for I am quite sure that this distinguished physiologist is clinically blind, and, I think I may add, wilfully so.

Stewart concludes his article in the bravura style so dear to all writers who stand foursquare on their pedestals of self-conceit:

"Mankind can apparently be divided into sheep and goats in regard to this matter, that is to say into sympatheticotonics and vagotonics, and the vagatonics have the better chance of escaping seasickness—if vagotonia and sympatheticotonia exist in ordinary, tri-dimensional medicine, and if seasickness is due to hypoadrenalism. But by my troth, as Mrs. Quickly has it, 'these are very bitter words' for the physiologist or the experimental pathologist—words like vagotonia and sympatheticotonia, hypo- and hyper-adrenalism, hypo- and hyper-adrenalinemia and all their cousins and connections. For he knows that in most cases they are but words, and in science words which conceal or even distort the facts do not leave a sweet savor in the mouth."

The writers whom Stewart takes to task and attempts to cover with ridicule have not distorted facts—they have merely reported occurrences as they encountered them. Nor has my effort to emphasize the importance of adrenal insufficiency in routine clinical experiences and correspondingly to attempt to mitigate both the factors which cause this depletion as well as to support the played-out organs, been based upon a distortion of facts.

There is nothing "suspiciously sweet" in the clinical considerations of this subject. Just because a certain person believes in a certain thing, and believes firmly, is no reason to advance the accusation that he is the victim of an "undisciplined imagination." But granting that Stewart is somewhat in the right when he says the disease of the clinicians in endocrinology is undisciplined imagination—I am granting the truth of this charge only for argumentative reasons—the same cannot be said in any attack on him, for he is the victim of a decidedly disciplined imagination—disciplined so thoroughly that it does not require any deep thinking to arrive at the conclusion that his article and Frank's article and several of Hoskins' articles and a number of unsigned editorials in *The Journal of the American Medical Association* are expressions of such striking similarity of thought that a family resemblance is quite evident and the motive underlying them has all the noble qualities of a secret pact and understanding.

III

THE

ORGANOTHERAPEUTIC "WILDERNESS"

"Where there is no vision, the people perish."—
Proverbs xxix, 18.

AN asseveration characteristic of old-fashioned physicians is to the effect that imagination has no legitimate place in medicine. Certain endocrinologists seem to be of a like opinion, asserting that imagination is fraught with danger since it may run away with the physician. Empiricism and unscientific medicine—its deleterious attributes—are emphasized in their arguments, especially when these undesirable "medical outsiders" obtrude themselves with suggestions regarding pluriglandular therapy. A matter to attract notice is the fact that during the last year it has happened frequently that the articles of some of my opponents have contained unmistakable insinuations coupled with their denials.

I am reverting here to George N. Stewart, of Cleveland—and I ask the reader's indulgence because of this since I am sure he must be a bit weary of my criticism of Professor Stewart's attitude—merely to illustrate how blurred his clinical vision is and how unfortunate it would be if every physician would believe him and thereby deny the clinical evidence reported by many physicians of standing in regard to the adrenal aspects of many toxic conditions.

"Where there is no vision, the people perish" is indeed a true saying, and applies just as well to medicine as to literature and the other arts. I would that Stewart were the possessor of enough vision to take an interest, a lively interest, in some of the possibilities of organotherapy. My desire for him to be thus dowered is born of the desire I hold toward every man of intelligence so that no longer may it be said of him that he walks in darkness. Were Stewart among those with a real vision, would he be guilty of the following?

"On the whole, then, it must be granted that hitherto the attempts made to evoke in animals a well-marked syndrome characteristic of adrenal deficiency, have been singularly disappointing. The contrast is great when we leave this desert, where the physiologists and experimental pathologists have wandered, striking many rocks but finding few springs, and pass into the exuberant land of clinical endocrinology, flowing with blandest milk and honey almost suspiciously sweet."

Merely because Stewart and his colleagues have no encouragement to offer is no reason, as I see it, why everybody else who does offer some encouragement should be wrong; and his statements remind me of an attitude which has not been uncommon in medicine, and for that matter in other sciences, the attitude of subtle criticism by those who when their attention is directed to some progress, have no good word for it or for the one responsible for it because they did not happen to think of it first.

Stewart's reference to a "suspicious" sweetness of the milk and honey of this endocrine land of promise immediately was taken up by the editor of *The Journal of the American Medical Association* who used this for the basis of another attack, which in turn was reproduced again by Hoskins in still another editorial in *Endocrinology*—forming a sort of vicious circle of opposition.

The criticism meted out to those who choose to believe in clinical adrenal insufficiency seems to agree with the editor of *The Journal*, for, in still another editorial, after having quoted the "wilderness" statement he concludes:

"How much longer will our profession continue to merit such criticism? Just so long as our profession continues to give serious consideration to pseudoscientific rubbish promulgated by exploiters of organic extracts."

In passing, be it remembered, that none of these writers admit that they have given careful clinical trial to the suggestions or preparations they so lightly malign. They have not ventured out of this wilderness, as did the Israelitish spies, into the promised land, and they cannot return with their proofs of the riches and fruitfulness of the land. They merely are sure that the grapes are too big to have any flavor and that the tales told are the products of "undisciplined imaginations".

No discovery has yet been made that has not had its opponents in the beginning—its pessimis-

tic critics who have cried aloud at the innovation. And no new note has been introduced in literature, music, painting or sculpture that has not fared in the same manner. To cite only a few instances, I would mention the brutal criticism of *The Edinburgh Review* in connection with John Keats' immortal poem "Endymion"; the hissings and derisions that arose against Richard Wagner's first operas; the laughter visited on Whistler and the shouts of denunciation against Auguste Rodin, France's immortal sculptor.

A like attitude obtains in medicine every time a new idea is put forward by a well-meaning man attempting to further our knowledge of these problems which are still in the land of shadows. Lord Beaconsfield had a poor opinion of critics, for he was the father of a clever epigram on the tribe; namely, that "critics are men who have failed in literature and art". Would it be unwise to say of the unkind critics whose criticisms are displayed in this little volume, that they too are embittered because they have failed in medicine—failed in keeping up with its progress? Or would it be less cruel to attribute their exceedingly unfriendly attitude to the fact that, being human, they are a bit jealous because the ideas did not come to them first? I leave this problem to those who have more leisure time to solve it than I, and who also have a more penetrating mentality than is mine.

But this "wilderness" visualized by Stewart, fortunately is of a transitional nature; the Promised Land is no longer a fiction but an actuality. From Mount Pisgah it was seen more than ten years ago by Dr. Leonard Williams, of London, in an introduction prepared at my request for a special "Hormone Therapy" issue (April 1913) of *The Prescriber*, Edinburgh, which I had the honor to suggest and assist in preparing:

"Yesterday was the day of the pathologist, more especially of the bacteriologist. The day before yesterday witnessed the triumphal progress of surgery. Physiology and medicine, all wrung in the withers and quite chapfallen, contented themselves, perforce, with the crumbs that fell from the rich microbic tables of these others. But the whirligig of time brings in his revenges. Today and tomorrow, and the day after, are foreordained to the physiologist, the physician and the therapist. Their hour has come through the agency of the internal secretory glands, which already unfold before the astonished view of the seeing eye, a land of promise beside which the vast territories conquered by Lister and Pasteur are destined to pale into honorable insignificance. The ductless glands and their hormones come to us as peaceful conquerors who brook no denial. They lighten our darkneses and show us miracles. In studying them and endeavoring to unravel their intricate and esoteric mysteries, one seems ever and anon to be on the trail of the Great Secret, and in danger of losing one's mental perspective."

This "transition" is a matter that rests with

him whose faith is such that he is dissatisfied with the "wilderness" and who, brooking no denial, longs to extricate himself from its paths that lead nowhere and get out into the open where all is sunshine, and he who runs may read. It does not require a superior intellect to rid oneself of the tangles which beset all who still live in the "wilderness". Any physician of average intelligence can enter this Promised Land at once and profit by the experience of those whose words are not written small in the annals of pluriglandular therapy. And it is not only the experience of others which will count in the Promised Land; ere long his own experience will be of such value to him that no regret will be his for having "foolishly" and "heedlessly" entered a province which has been tabooed by all those who are closely related to the "din" and "noise" makers who clamorously have denied, from time immemorial, worthiness and value to anything new in medicine.

IV

THE

"SUPPOSITITIOUS PITUITARY INFLUENCE"

"All that is human must retrograde if it does not advance."—Gibbon.

IN this chapter an exceedingly pleasant undertaking devolves on me in the matter of telling the reader a thing or two about Dr. Robert T. Frank's interesting studies in regard to the ovary and the internal secretion of the sex organs. Let me emphasize here that Dr. Frank is considered by many to be an authority on the subject.

Considerable original research work characterizes Dr. Frank's papers and the clinical and experimental applications of organotherapy are both interesting and novel. Witness thereof is his paper on "The Ovary and the Endocrinologist" in *The Journal of the American Medical Association* of January 21, 1922, p. 181.

Dr. Frank's article starts bravely in the following manner:

"The ovary exerts a powerful influence on both the primary development of the female sex organs and their function during sexual life. Whether other glands of internal secretion affect the sexual sphere, except secondarily, that is, by intermediation of the ovaries, is more than doubtful. For example, the claims of Goetsch that anterior lobe pituitary extract stimulates the growth of the sex organs was disproved by me in 1919 and more recently again by Sisson and Broyles. Yet

this supposititious pituitary influence continues to crop out in the literature and in the 'therapeutic advertising pamphlets with which the medical profession is bombarded.'

It is open to considerable doubt whether this "disproving" of the work of Goetsch, and a score of other investigators, by the way, will be accepted by the majority of the profession, even though, according to Frank, his work published in 1919, apparently has been supported later by that of Sisson and Broyles working in the same laboratories at the Johns Hopkins Hospital where Goetsch did his splendid work. It must be remembered in this connection, however, that the work of these two writers concerns "The Influence of the Anterior Lobe of the Hypophysis on the Development of the Albino Rat." And while it is perfectly true that Goetsch's claims concern the stimulation by organotherapy of the sex organs in animals and that Sisson and Broyles also have done their work with animals, we are only interested incidentally in the influence of the pituitary on the sex glands *in animals*, for our chief interest is in regard to the effect the pituitary gland exerts upon the ovaries in women in a clinical way.

The three words—"supposititious pituitary influence" (upon ovarian function) are talismanic and should be remembered as such, for by writing them Frank declares himself at odds with the

numerous statements which have been made connecting pituitary dysfunction with dyovarism, as well as pituitary therapy as a possible means of regulating functional ovarian difficulties. In short, he has the temerity to discredit them as figments of the imagination.

The second paragraph of his article yields nothing in interest to the first—in fact, is an improvement over it in that he declares himself before the public the victim of a degree of humor of which he is not conscious.

“No matter how often a plausible appearing claim is shown to be wrong, if it appeals to the imagination or meets with the desire of the therapist for new and dramatically effective agents, the falsity continues to be accepted. The results of incomplete experiments, isolated empiric observations and fantastic hypotheses are thrown together to form a glittering and ever changing kaleidoscopic picture. A new terminology is being coined. Shotgun mixtures containing the ‘fifty-seven varieties’ are being circulated. What is to be the end of this seemingly uncontrolled wave of mysticism, hysteria, commercialism and credulousness? Does it betoken the birth of another medical cult, to be controlled by the charlatan and self-seeker and which, at least for the moment, will carry along with it the overoptimistic, the uncritical and the untrained members of the profession? If this must be the outcome, the sooner the break occurs the better; then all hail to the ‘endocrinopractor’! The profession is well rid of him, but let us at least try to save the un-

wary, whom he is at present deluding and perverting."

It is evident that Dr. Frank has a burden quite similar to that of some of the gentlemen whose names are referred to in other "adventures," and that the reason for the publication of his article is not so much his desire to analyze or elucidate the influences exerted by the ovaries on the genital sphere and on the body as a whole, as to serve as propaganda, for the large part of the remainder of Frank's paper consists of a repetition of a number of things, most interesting things too, that he has written previously, and refers to work which he has done quite some time ago, which is none the less splendid and entirely creditable. Incidentally, no further consideration is given in Frank's remarks to the influence that the pituitary is supposed not to play upon the sex glands. In other words, he does not find any opportunity to establish the veracity of his statement that the pituitary influence upon the sex glands is, as he calls it, "supposititious."

A few comments are really necessary here so that the reader may be able to draw a heavy line between what is "fustian" in writing and what is expressed thought born of a commanding degree of mentality. No doubt you have been impressed in the theatre or in your reading by speeches which dripped with blood, which tore deep rents into your sense of right, which have brought tears

to your eyes because you felt that the hero or heroine was so greatly the victim of Fate as Fate was spun by the machinations of the villain. This dire state of mind is the sort that every intelligent man is ashamed of *afterwards*—he feels that it was unmanly for him to have been moved to heights of enthusiasm or plunged into depths of despair—he cogitates just why the thing affected him the way it did. And he forgets that deep down in his heart there is a “soft spot” for the melodramatics of life. No doubt, Dr. Frank is no better and no worse than the man who has just been pictured, and no doubt when he wrote the lines quoted he was in the fierce clutch of the “melodramatics”, was fascinated for the moment by what he had in mind to write, and afterwards was heartily ashamed that he had ever allowed himself to be guilty of such a travesty of literature. “He wrote from his heart,” we can hear his friends exclaim directly they read the article and were still under its spell; but a few days later a few may have said: “He wrote from his liver.” And sometimes the minority are right.

One more quotation from Dr. Frank’s paper should suffice to illuminate the reader so thoroughly as to his prejudiced attitude that all further excerpts are superfluous. Here are the last paragraphs:

“This leads me to state that today we have no better ovarian extract on the market than we

had in 1910 when I first discussed this subject. The commercial preparations are 'degreased' or 'defatted' and therefore deprived of such minute doses of the active principle as they originally contained. Pharmacologically they are inert. This includes the ovarian extracts, corpus luteum extracts, ovarian residue and ovarian substance, etc., of which we read they cure amenorrhea, sterility, dysmenorrhea, menorrhagia, metrorrhagia, pernicious vomiting, climacteric disturbances and mental confusion in women, etc.

"The near future may supply us with an at least partially potent liquid extract. In the meantime, it seems likely that we shall continue to receive ecstatic reports from the commercial laboratories of the marvelous cures obtained with ovarian extracts, especially if combined with a pinch of thymus, spleen, bone-marrow and pancreas. . . . The ovarian extracts now in use have been deprived of the small amount of active substance that they have contained when fresh. Their pharmacologic effect on the sexual tract is nil. This does not imply that a total extract cannot be elaborated."

So all commercial ovarian preparations are "pharmacologically inert"! A mountain was in labor and brought forth a mouse. And in this case the mouse is a sickly animal and cannot thrive, for only truth is nutritious. The "ecstatic reports from the commercial laboratories" is an empty phrase for the man in the stalls of our medical theatre and a sweet morsel for the gallery. Of course, the gallery will applaud with

hands and feet, will shout "Bravo"—and will carry home fond recollections of this jumble of words and repeat them verbatim. The gallery "loves" attacks on commercialism; its simplicity of thought always bespeaks a friendly reception for the word. But who would want to sit in the gallery knowing its component parts? How about the intelligent spectator? Would he crave a change from the stalls? I doubt it.

It happens that a short time ago I was talking about Doctor Frank's article to the editor of *The Journal of the American Medical Association* in his office when his associate, Doctor Fishbein who was also present, informed me that they had had several letters criticizing this particular statement in Frank's paper, but that they could not be responsible for it because it was in an original article; and Doctor Fishbein then informed me that there was in the Correspondence Department of the current issue of *The Journal* an article coming out and opposing Frank's attitude; and since I had been traveling and had not seen *The Journal* (for March 11, 1922), on my return to the office I found a clipping from it awaiting me on my desk, and here it is:

The Ovary and the Endocrinologist

"To the Editor:—May I comment on an article entitled 'The Ovary and the Endocrinologist,' by Dr. Robert T. Frank, which appeared in *The Journal*, January 21? I have been hoping that someone interested in the subject and realizing the

benefit from certain types of organotherapy, might answer Dr. Frank's rather scathing remarks anent the subject of ovarian organotherapy. I will agree that the rank commercialism which has enveloped the field of endocrinology has done much to discredit it. I have no use for the exploiter of the 'shotgun mixtures,' or the pluriglandular products, put upon the market and foisted upon the profession by means of 'therapeutic' advertising pamphlets, postcards, etc. Dr. Frank's allusion to the 'endocrinopractor' is well made. I must take issue with him, however, in regard to ovoid therapy of a rational and common sense type. I cannot understand his pessimism. When he says that corpus luteum extracts, ovarian extracts and ovarian residue are inert, and shows his disbelief that beneficial results are obtained in the functional amenorrheas, certain types of dysmenorrhea and in the treatment of the symptoms of the artificial and physiologic menopause, I believe that the products he used have either been of poor preparations, not fresh, *or that his therapy has been incomplete.* Ovarian organotherapy must be prolonged, continuous and regularly applied to obtain results, and fresh glandular products must be used. The miraculous effect of luteum extract in amenorrhea of the functional type, combined with thyroid extract where obesity is coexistent in dysmenorrhea, not referable to mechanical causes and in the early symptoms of the menopause, is too well known to me and many others to allow Dr. Frank to discredit it without a word of protest.

ADAM P. LEIGHTON, JR., M. D."

Portland, Maine."

In passing let the reader take note of the pregnant phrase about the possibility that Frank's pessimism about ovarian organotherapy is because "his therapy has been incomplete," as I have taken the liberty of italicizing it. *That is just the point!*

It may be noted here that the conscience of the editor of *The Journal* was soothed a little because Leighton makes use of his opportunity to hand out another "slam" to those whose ideas and methods differ from his. He could not help, however, slipping in a couple of hints about the pluriglandular idea!

Perhaps it will be well at this time to call attention to some of the statements that have been made emphasizing the relation that the pituitary gland bears to ovarian function, because I do not think that any physician, no matter how intelligent and highly placed, can with one statement dispose of all the clinical experiences of literally hundreds of investigators.

The pituitary gland most certainly exerts a very decided and clear-cut influence upon sex gland development and functioning. The individual who has pituitary insufficiency invariably manifests a genital phase, so much so that the so-called "Froehlich syndrome" is known in other terms as the "adiposo-genital dystrophy." Every book bearing upon the pituitary gland and practically every comprehensive article on the subject

calls attention to the indubitable fact that disorders of pituitary functioning very often are made manifest through derangement of the function, and even the development and structure, of the sex glands and adnexa. It is a fact, too, that this is one of the early manifestations and, consequently, is of prime diagnostic value. And it is a source of great satisfaction to me to have been able to emphasize the pituitary aspects that so commonly are present in ovarian dysfunction, thereby broadening the possibility of treating an ovarian syndrome by ovarian extract or corpus luteum, to which pituitary therapy is added.

In other words, since Frank does not agree with me that a "shotgun" combination of thyroid and pituitary and ovary, with corpus luteum, is a more suitable remedy than the administration of ovarian substance alone, he must needs attempt to discredit me scientifically and he attempts to do so by referring to this "supposititious pituitary influence," and also insists that all commercial ovarian products are inert, while as a matter of fact in both instances he is absolutely wrong.

I have gone into this matter quite a bit since this remarkable statement came to my attention and find that there are at least forty-five papers by various authors in a half dozen different languages, and thirteen books in my library in which this pituitary-ovarian relationship is taken up quite fully, and in which information is given

both of an experimental laboratory character—animals being used in the work—as well as of a clinical and hospital nature (in the treatment of disease) which indicates that the influence of the pituitary gland upon the gonads in both sexes is as definitely proved as that of the thyroid, which, by the way, is an equally important factor in any endocrine gonad dysfunction.

Still greater emphasis can be added to this if necessary, because there are a number of articles by this same Doctor Frank indicating that his experience with organotherapy—"ovotherapy" as he calls it—is both interesting and instructive. He has been in the habit of using organotherapy for some years and has not hesitated to say so. How inconsistent then is his present attitude?

This same Doctor Frank read a paper on "The Clinical Manifestations of Disease of the Glands of Internal Secretion in Gynecological and Obstetrical Patients" at the meeting of the American Gynecological Society, May 21, 1914. His complete article, supplemented by a bibliography of 136 items, was published in *Surgery, Gynecology and Obstetrics*, November 1914, xix, p. 618. In the seventh section of this article entitled "Clinical Manifestations: Local and General" the author commences by making the statement that

"The interrelation of the glands of internal secretion, the detailed description of the physiological and pathological genital function of the ovary . . . were described in detail because,

without this preliminary, intelligent discussion of the clinical manifestations is impossible."

He then divides this subject into several headings, each with several subheadings. We are interested particularly in the first heading, "Genital Inactivity (Hypofunction)" and a few quotations from Frank's remarks will be made. Under the subheading "Congenital Conditions," he states that the true infantilism must be placed in a class by itself "Because the defect . . . may be multiple, affecting different glands of internal secretion simultaneously, in such a way as to defy analysis and detection."

Under the second heading, "Apparently Primary" he admits that

"Upon careful consideration, the experienced gynecologist must realize that he has seen few cases . . . which do not show abnormalities pointing to disturbance in other glands of internal secretion . . . Whether the disturbance is primary in the ovary or secondary to distant troubles does not always become apparent."

Again under the subheading "(c) Secondary Sex Characters," it is stated that

"Defects or changes in the secondary sex characters occur frequently. They take the form either of the adult eunuchoid type (hypophyseal?), or show a tendency toward male characteristics (species type of Tandler and Grosz) (adrenal or hypophyseal overactivity?)"

and the writer then divides these into several

classes, indicating the usual clinical findings and referring the reader for further details to the books by Tandler and Grosz ("Die biologischen Grundlagen der sekundären Geschlechtscharaktere") and Falta ("The Ductless Glandular Diseases".)

Admittedly, thus far Frank is not very decided in his assurance that there is a hypophyseal or pituitary influence upon the genital function and dysfunction, but he seems to be thoroughly convinced at least about the importance of considering the relations of the glands of internal secretion, which is worth something.

In considering the third division of the clinical manifestations, "Surely Secondary," Frank continues:

"The local genital findings are as in the previous class, but unmistakably secondary to thyroid disease (Graves' disease . . . cretinism, myxedema), hypophyseal disturbances (acromegaly, Froehlich's syndrome—dystrophia adiposogenitalis), destruction of the adrenals (Addison's disease), or thymus persistence (status thymolymphaticus and infantilism). The symptoms of the primary affection usually overshadow the secondary genital changes completely."

I feel justified in presuming from the quotations that I have made that Frank admits that there is indeed a pituitary influence upon ovarian function and dysfunction and, therefore, that he was wrong in referring to this reality as "supposititious."

In passing, another statement made in one of Frank's later articles ("Symposium on the Relation of the Glands of Internal Secretion to Gynecology and Obstetrics." *Surg. Gyn. & Obst.*, September, 1917, xxv, p. 228) indicates a possible reason for his sweeping criticism of the supposititious inertness of commercial ovarian preparations. He writes:

"All those commercial extracts (and these are the extracts which are employed in the clinical articles reported), which the writer has examined, have proved inactive biologically, *using the growth effect exerted on the rabbit uterus as a test.*" (Italics mine.—H. R. H.)

A brief explanation is necessary here. We do not test commercial ovarian preparations in clinical practice by trying their effects upon the growth of the rabbit uterus. They are administered for therapeutic purposes to sick people!

I do not doubt that there will be a good deal more discussion of this particular subject. However, Frank is not the only one who has been interested in the development of organotherapy and the preparation of remedies from the ovaries and I am afraid that in addition to impugning the veracity of the opinion of our unwilling friend Adam P. Leighton, Jr., of Portland, Maine, whose opposition to Frank's attitude has been referred to above, he will have to undo the entire clinical work with ovarian therapy of many scores of

workers including such American writers as Howard A. Kelly and Curtis T. Burnam of Johns Hopkins, John C. Hirst of Philadelphia, Oliver T. Osborne of Yale, Wm. P. Graves of Boston, Samuel W. Bandler of New York and Wm. Engelbach of St. Louis, as well as a very much larger list of authorities abroad. Those men are not staking their reputations for the sake of a figment, a crotchet or a desire to achieve the sensational. Their probity is undoubted and their written words are not negligible. Whose opinion in all truth should take precedence—that of the unbiased investigator or that of the biased? I leave this “riddle” to the reader for solution.

As the MSS. for this book is being completed I have received from my Paris agents a new book by Léopold-Lévi entitled “Opothérapie Endocrinienne: Ses applications journalières” (1922). In chapter three (page 57) there appears the following:

“Pituitary organotherapy is admissible, too, in pluriglandular endocrine syndromes in which the pituitary is involved. Developmental and functional disorders of the sexual system should also direct attention to the pituitary gland, as also to the thyroid. In man, there is agenesis, absence of puberty, developmental infantilism or reappearance of infantilism, return of puberty. In woman, there is amenorrhea which, according to Hofstatter, can be classified according to whether there is genital aplasia, infantile uterus, hypoplasia in multiparas, or whether the amenorrhea is con-

secutive to toxi-infections or manifold and prolonged lactation. In these cases the therapeutic effect of pituitary organotherapy is indirect (Renon and Delille) but at the same time excitatory."

The author of this book has been clinically interested in this subject for many years, and his new book happens to be his fifth on endocrine subjects. His opinions evidently also disagree with some of those under discussion in this chapter.

In closing this chapter a statement might be made in partial justice to Doctor Frank, certain of whose opinions I have taken so decidedly to task. A colleague, who like myself was astounded at his article, wrote him a letter. (So did I, but he did not answer it.) He answered the colleague, however, and in the course of this letter which has been shown to me, he says, "The pituitary gland has a very marked influence on ovarian function. What I have shown is that *pituitary extracts* as now available and used have not the effect ascribed to them." But that is not what Doctor Frank says in his article and he does not give any evidence to show that pituitary therapy with the "extracts as now available" does not measure up to the usefulness claimed for it. He makes specific statements regarding the supposititiousness of the pituitary influence, and then to add insult to injury he denies absolutely the thera-

peutic value of commercial ovarian preparations even though in the quotation from my friend's letter he now fully admits that "the pituitary gland has a very marked influence on ovarian function"—as I think has been shown very clearly both here and elsewhere.

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V

HARROWER'S HYPOTHESIS AND HOSKINS' HALLUCINATIONS

"Error of opinion may be tolerated where reason is left free to combat it."—Thomas Jefferson.

AS indicated in the Introduction, the fundamental principle upon which the work of The Harrower Laboratory has been builded, is what is sometimes called "the pluriglandular theory." This is fully outlined in Section 2, Chapter 4, of my book "Practical Organotherapy," the third edition of which recently has come from the press.

Briefly, this idea involves the importance of the relations of the glands of internal secretion. It does not seem possible that any generalized influence for harm that may come about in the course of disease can be limited in its effects to a single endocrine organ. Again, if there is a decided disturbance in one of the glands of internal secretion, as for example, the thyroid gland in myxedema, there cannot but be a reflex influence as a result of this upon the other endocrine glands which are related to it physiologically.

I believe that the glands of internal secretion are in so intimate a relation with each other that, as I have often said, "there never was a purely uniglandular endocrine disorder," and that much of the success that has come to those who

have followed the ideas which we have developed, has come about because of the fact that pluriglandular therapy was used instead of single gland extracts.

In my publications I have dwelt on pluriglandular therapy so fully that mere mention of it here is all that is necessary. But a more extensive account should be given of an hypothesis which I devised so as to make clear to myself certain clinical experiences which I had noticed very frequently following the use of pluriglandular remedies.

This "Hypothesis of Hormone Hunger," as I called it, was worked out by me, and first discussed in an article in the *New York Medical Record*, August 16, 1919. The philosophy of this hypothesis is as follows:

"Each organ of the body that is dependent upon hormone influences must have some subtle capacity to pick up the hormones from the blood as they float by. This cannot but be true, else how could the passing 'chemical messengers' bring about the influence upon the organ or cell that they are supposed to affect? Not only must there be a definite capacity to pick up these hormones as they are brought to the cell by the blood, but there must be a selective capacity, for the blood contains all the hormones that we know of as well as probably a good many more that we do not know at present. I do not feel that the imagination has to be stretched very much to presume that there is a remarkable 'cellular judgment' or selective capacity to pick out the hormones

which are needed—and in the amount they are needed.

"It is with this particular selective power in mind that I have developed this hypothesis of hormone hunger. I contend that under varying circumstances these cells must be more active in their picking up of the passing hormones than at other times. In other words, at times a condition of hormone hunger actually must be present. Let me explain: Take as an example the thyro-ovarian interrelationship—this is, perhaps, the most thoroughly established and most easily understood. It is well known that there is a principle produced in the thyroid gland which exerts a very marked influence upon ovarian function. (It will be recalled that in myxedema there are definite functional ovarian disorders, that girls with goitre very often have serious menstrual difficulties and, finally, that the cretin, who has no thyroid gland, does not develop sexually.) Surely it is fair to believe that there is a principle made in the thyroid which stimulates ovarian function, and that this must necessarily reach the ovaries through the blood, and of course, that the ovaries must have some means of getting hold of this hormone. If, then, this thyroid hormone passing through the ovaries in its blood supply happens to be deficient, after as much of it as can be found is taken up by cells of the ovary, and the demand is greater than the supply, there will remain a need for that which is not present, i. e., the ovarian cells will be 'hungry' for more of the thyroid stimulus. Furthermore, this 'hunger' will vary, depending upon the degree to which the thyroid is functioning and the hormone needs of the ovary."

The foregoing statements have aroused considerable comment, mostly favorable. A gratifying feature has been that several editorials in approval of my theory have been published and that an encouraging number of writers have referred to it in the course of their articles. Of course not all the comments in regard to this idea have been favorable. Perhaps one of the most active opponents of this idea is the editor of *Endocrinology*, Dr. R. G. Hoskins, who, in a number of original articles and signed editorials, has attempted to throw cold water on my enthusiasm, and to prevent some of his colleagues from being "misled" by me. Dr. Hoskins credits me with having had much to do with the development of the science which he calls "pseudoendocrinology," and feels that I am leading the medical profession astray, and should be stopped in some way, even if it is necessary to plow up the entire field of endocrinology in order to start over again, untrammelled by so many of the misstatements with which I am credited.

In a signed editorial published in "*Endocrinology*" entitled "What is Endocrinology?" Dr. Hoskins has this to say:

"There is a class of writers who affect the term 'so-called endocrinology,' the implication seeming to be either that the existence of endocrine organs is doubtful or else that the voluminous literature pertaining to them is of such uncertain significance as not to deserve formal

recognition. That the literature does include an intolerable deal of twaddle, no well-informed reader can deny. Such pretentious nonsense might well be designated pseudoendocrinology.

"The proponents of this sort of literature are coming in for criticism on all sides. A recent editorial in *The Journal of the American Medical Association* concludes: 'How much longer will our profession continue to merit such criticism? Just so long as our profession continues to give serious consideration to pseudo-scientific rubbish promulgated by exploiters of organic extracts.' The writer might well have added: 'and by clinical incompetents seeking easy paths to fame.'

"Upon the members of the Association for the Study of Internal Secretions a special responsibility devolves lest a long-suffering medical profession in disgust with the rank growth of weeds in our fertile field in reformatory zeal uproot wheat and tares alike.

"It fortunately happens that the pseudoendocrinologists have developed such a characteristic array of methods that they are relatively easy to identify. They are strikingly addicted to theorizing. If, in a given article, the 'explanatory' portion bulks larger than ten or twenty per cent. of the original data adduced, one is rarely in error in classifying it as 'pseudoscientific rubbish.' As Elliott has sagely remarked: 'Medicine owes no thanks to him who, without proof, would formulate her theories.' Those who are attempting to elicit our gratitude in this way often put forth the specious plea that they are pointing the way to research,—as though the competent investigators in this field were not beset with an almost bewildering array of problems.

"The pseudoendocrinologists are much given to appeals to 'physiology.' But the physiology cited, one seeks in vain in any first class treatise on that subject. The guesses of novices and the deductions of shallow thinkers are habitually quoted as on a par with substantial facts. Gross distortion of the evidence is constantly encountered. Such data as support the preconceived theories of the writer are cited while opposing data are ignored. This is not infrequently carried to the point of actual mendacity. Systematized delusions masquerading as the 'teachings of experience' are not uncommon. Marvel mongering is also an earmark, though this is going out of style.

"Examples could be cited by the volume. One recent paragraph, and it by no means the worst available, may be quoted: 'I have frequently been asked why adrenal gland and pancreas can be given together in hyperthyroidism. . . . This is readily explained. . . . Adrenal extract is a cardiac tonic and slows and strengthens the heart. Further, when administered in this form, its influence upon the adrenal glands and the factors controlled by them is supportive rather than stimulative. . . . In the complex hormonal mixture in the blood all the hormones, both antagonists and stimulants, are to be found and the remarkable selective capacity of the organism to avail itself of those which are needed, and in proportion as they are needed, explains why, when antagonists are given simultaneously, benefit may accrue in both directions represented by the opposing principles. Suffice it to say that. . . . the antagonistic value of pancreas over adrenal medullary irritability, as well as the thyroid itself, makes the pluriglandular idea not so unreasonable after all.'

"Space and patience are lacking for a full analysis, but a few of the violations of sound physiology may be indicated. That adrenal extract given by mouth has any effect on the circulation is without evidence that competent pharmacologists can now accept. 'Its influence is supportive rather than stimulative' is only verbalism that obscures rather than clarifies. The 'complex hormonal mixture of the blood' is quite possibly nonexistent. In few cases has it been proved that the endocrine organs contribute anything to the blood stream. They may function by a process of subtraction rather than addition. Hormonal 'antagonists' are, so far as proof is concerned, largely mythical. That epinephrin is rapidly destroyed in alkaline media and that pancreas extract is alkaline comprise the sum total of clean-cut evidence on the point. The 'remarkable selective capacity of the organism' is, so far as can now be determined, a mere figment of the imagination, which is being grossly overworked as an excuse for haphazard, pluriglandular dosing. If the body cells were possessed of any such critical acumen as postulated, why should we ever encounter a case of acromegaly or hypothyroidism? It is definitely proved that the cells will take up thyroxin or epinephrin in lethal quantities, when exposed to excess of these substances. Finally, the 'value' of pancreas extract as a source of hormone is, according to reliable evidence, nil.

"That given endocrine gland substances may be valuable in given clinical conditions may or may not be true, as a matter of empirical observation. That enlightened empiricism may lead to further valuable therapeutic deductions is not improbable. Such results are to be expected, however, not

from promiscuous dosing with hit-or-miss mixtures, but from carefully controlled experiments carefully analyzed. Rigid critique and rigid logic are indispensable. Any data adduced must stand on their own merits as data. Confusing the issue by the introduction of impressionistic physiology is deplorable.

"In the endocrine field, as in all other fields of medical science, progress depends upon intelligent discrimination. Sound workmanship deserves every support, mere tinkering, none. Pseudoendocrinology will disappear as soon as it ceases to be profitable. The medical profession at large can alone determine when this time will arrive."

It is difficult to know what to say when confronted with so much abuse. Hoskins' criticism that the pseudoendocrinologist is 'much given to appeals to physiology' but 'one seeks in vain in any first-class treatise on that subject' is unfair, for *clinical physiology* is surely a real thing. There is plenty of proof also that this is not true, but it really seems that those who feel with Hoskins are not so much concerned about physiological reactions in sick persons, but rather are interested more in laboratory experiments, which occasionally they are unable to duplicate, as for example, the experiences outlined by Geo. N. Stewart elsewhere, and previously considered in another adventure. We are looked upon as "novices and shallow thinkers" (Chapter II), and as "constantly and grossly distorting the evidence." And if by any chance we choose to quote some

clinical experience of an unusual character, then we are called "marvel mongers."

A few of Dr. Hoskins' statements invite attention. He indicates that adrenal extract given by mouth is without effect on the circulation, simply because competent pharmacologists cannot accept the evidence of the clinician. Fortunately, the patients who come to us for treatment do not expect us to treat them as though we were pharmacologists, and there is plenty of evidence in a hundred different papers that adrenal therapy, that is to say, the administration of desiccated adrenal substance by mouth, not merely has an effect upon the body, both in health and disease—chiefly in disease—but that its chief influence is upon the circulatory mechanism of the body, as manifested on the blood pressure in particular.

The "verbalism that obscures rather than clarifies," which refers to my statement that the influence of adrenal substance "is supportive rather than stimulative," deserves consideration for a moment. (And, by the way, the criticised pluri-glandular formula containing adrenal and pancreas substances which is used in the hope of controlling a part of the extreme sympathetic irritability and heart hurry was first suggested by André Crotti, of Columbus, Ohio, an old time assistant of the famous Kocher of Berne *and a clinician*. My *Pancreas Co.* which has been used successfully in many cases of hyperthyroidism is a slight modification of Crotti's original formula.

If an individual is suffering with an asthenic state, strychnin is very often recommended as a means of stimulation, and under certain circumstances it is of decided therapeutic value. This influence is conceded by the pharmacologist as well as the clinician, to be of a stimulative character. On the other hand, if an individual is asthenic and tired out in conjunction with a serious degree of adrenal insufficiency, and we administer the indicated organotherapy, or "adrenal extract," e. g., the total gland, it is not very difficult to conceive that such stimulation is not to be compared with that which we get from strychnin. In other words, it is not really stimulation, because stimulation involves a sort of an irritation. As a matter of fact, when the body reacts to strychnin it is in a well-intentioned effort to dispose of a poison which the body has discovered to be present, whereas when we give adrenal substance to a person with hypoadrenia, we are not stimulating it, but supporting it, just as we "support" a tired-out horse with a bag of oats, instead of whipping him. I think that there is a real difference; and so do others who have been willing to make a similar comparison in a clinical way.

Attention should now be concentrated on Hoskins' reference to "the remarkable selective capacity of the organism"—a quotation, by the way, from one of my articles. He insists that this is

"so far as can now be determined, a mere figment of the imagination which is being grossly overworked for haphazard pluriglandular dosing."

He then attempts to explain the absurdity of his position by saying,

"If the body cells were possessed of any such critical acumen as postulated, why should we ever encounter a case of acromegaly, or hyperthyroidism? It is definitely proved that the cells will take up thyroxin or epinephrin in lethal quantities, when exposed to excess of these substances."

First of all, in pluriglandular therapy and even in the administration of single glandular extracts we do not offer "lethal quantities" of these products. The conditions which are present in hyperpituitarism or even hyperthyroidism, do not happen to lend themselves particularly to any kind of glandular therapy, much less to pluriglandular therapy; and while without a doubt excessive amounts of thyroxin or adrenin can cause serious symptoms, indicating that the cells can take up "lethal quantities" when exposed to an excess of them, as Hoskins indicates, he is introducing a factor which is not germane to the subject.

This would seem the proper place to republish a letter received by me late in 1919 from Dr. R. G. Hoskins, now of Columbus, Ohio, which is really a comment on the reprint of my article referred to above, which I sent to him as editor. This letter was originally published with his ac-

quiescence in *The Organotherapeutic Review*, (January 1920, vi, p. 62) :

"Thank you for your interesting reprint of your 'Hormone Hunger' paper. So far as I can see, it is perfectly good biology; it is rather demonstrated fact, however, than theory. You are somewhat too modest in applying it merely to hormones. Precisely the same mechanism—whatever it may be—comes into play when a young bone cell has to pick out calcium or an active muscle, glucose, from the blood. One can call it 'hunger,' 'specific affinity' or whatnot. Your term has the advantage of graphicness."

We all know what the whirligig of time may effect, but my casual readings have failed to bring home another instance in which there is such a diversity of opinion from the same source in the course of so very few years. Perhaps after all Dr. Hoskins was not strong enough to hold out against "*the word from above*."

This hypothesis of hormone hunger is a well-intentioned attempt to explain how it is that various parts of the body are able to utilize certain hormones when it is presumed from the symptoms that these hormones are deficient, and I assert without any fear of contradiction that clinical experience shows that in these persons, the capacity of the cells to avail themselves of the previously missing and artificially replaced substances indicates that there must be some sort of a hunger, as I have called it, to facilitate their

appropriation. Now what might be called an excess, that is to say, the organotherapeutic administration of just a little more than the body may need at the time of its exhibition—not the persistent administration of undue amounts of thyroid extract, as has been done many times unfortunately, and which causes thyroidism, nor “lethal quantities”—is permitted to remain in the circulation until oxidized, or disposed of in the usual manner.

Just because we cannot explain the whole of the factors involved in organotherapy and endocrinology, is no reason why we should cast aside the whole theory until we are perfectly informed regarding all the details.

The fact does remain that there must be varying degrees of interest on the part of the various cells of the body for certain endocrine products which we may offer to them in the course of our therapeutics, and provided we are reasonable in the extent and character of our pluriglandular menu, without a question we are going to accomplish a great many remarkable things with our “haphazard pluriglandular dosing,” even though it may be based upon what Hoskins chooses to call “impressionistic physiology.”

The patients are not concerned in regard to the impressionism, nor are they always interested in the technical duplication of experiences in the laboratory, and if they can get some satisfaction

from the service of a doctor who is willing to give them the benefit of the possibilities of organo-therapy, and especially pluriglandular therapy, they are going to give what credit comes to the one to whom credit is due and not to the one or ones who are heaping ignominy on the heads of those who know that they are rendering help to their patients.

In order to emphasize his point, Hoskins states that the value of pancreas extract as a source of hormone "is according to all reliable authorities nil." Is it possible that the editor of *Endocrinology* has turned his back on the French literature on the subject as well as on the reports of such men as Combe of Geneva, Lépine of Lyons, Zuelzer of Berlin, Crofton of Dublin, Pochon, Carnot and Hédon of Paris, Biedl of Prague, and others? As a matter of fact, the possibilities of pancreas therapy in functional high blood pressure, sympathetic irritability, diabetes mellitus and, perhaps, in other conditions, represents a phase of endocrinology which deserves very much more study than has been given to it as yet, and there are at least two hundred papers having a bearing on this subject, many of them concerned with the experimental aspects of pancreatectomized dogs, as well as the clinical aspects of individuals with glycosuria.

No editor of a journal devoted to endocrinology should lay himself open to the charge of not being

versed in what the European profession is doing in the realm of endocrinological investigation, for no matter how limited his knowledge of the French language may be, his editorial acumen should be of so high a degree that no literature is excluded from his survey.

Then Hoskins also refers somewhat slightly to what he calls, "empirical observation." He says "that given endocrine gland substance may be valuable in given clinical conditions, may or may not be true"—he hesitates to admit it point blank—"as a matter of empirical observation." He then continues, "that enlightened empiricism may lead to further valuable therapeutic deduction is not improbable," *and this is exactly the point that I have always contended.* That is to say, while empiricism still may be reprehensible in the minds of some, it is the only way in clinical practice, to apply ideas which have been developed in the laboratory, or in the clinical experience of others. The duplication of a procedure because it has been recommended highly by a certain investigator or group of clinicians, is simon-pure empiricism—"the practice of medicine founded on mere experience" (Webster), or doing what one has done previously in the hope that similar experiences may be obtained. Hoskins is averse to admitting that empiricism can be of any advantage, nevertheless it is my opinion that progress in medicine has been based more upon empiricism

than it has been upon the special brand of science which Dr. Hoskins seems to believe in.

No doubt by now the reader has a very clear conception of Hoskins' strictures on pluriglandular therapy and on those who believe in it. The rather detailed account that I have given was necessary so that the greatest light could be thrown on the subject. It is only by this method that results can be achieved—by which I mean, it is only by going into the details of a subject that the reader is benefited in that he gets into close grips with the views and opinions of the contending forces. Hence, no apology is necessary in this instance for my "verbalism" as Dr. Hoskins would express it.

VI

PROFESSOR CUSHING'S ALLEGORY

"It is not enough to know; we must turn what we know to account. It is not enough to will; we must do."—Goethe.

TEN years ago Dr. Harvey Cushing, then connected with the Johns Hopkins Medical School, wrote a 341-page book entitled, "The Pituitary Body and its Disorders" (J. B. Lippincott Co., 1912), which has been a source of very considerable encouragement to many physicians including myself, who have been interested in this mysterious subject.

The other day, when in Boston, I had the pleasure of meeting Doctor Cushing for the first time, and after I had asked him why he did not get out a second edition of his book, after so long a lapse of time, he gave me to understand that he was not going to get out another edition, and seemed to me to be somewhat sorry for ever having published it.

I then asked him if he would answer two questions for me, for reasons which will be found in Chapter IV of these "Adventures". I asked him first if he had any information confirming the relation between the pituitary gland and the ovaries, and was informed that he "could not answer that question"; and, second, if he had had any experience indicating that pituitary therapy exerted any influence upon ovarian functioning, and,

naturally, I received a similar unsatisfactory answer.

While Dr. Cushing was intensely courteous, it was very easy to see that we live in different spheres, think different thoughts, and express them in widely differing ways. In the course of our conversation, he referred to the ease with which the medical profession "could be made to believe most anything" that was told them and happened to mention the large emoluments which came to a certain doctor who promoted a remedy called "Peruna," and also made some remarks regarding the remarkable facility with which the strange views of a certain defunct Bostonian were accepted by so many apparently intelligent persons throughout the country. Doctor Cushing was kind enough to assure me that he was not comparing the success of my work with that of the maker of "Peruna," but none the less it was apparent to me that he thought of me as one of the same class.

All of which is introductory to a consideration of an allegory which Cushing prepared as a presidential address which was delivered before the Association for the Study of Internal Secretions last June (1921). The whole trend of this allegory, which is entitled, "Disorders of the Pituitary Gland, Retrospective and Prophetic," and which was published both in *The Journal of the American Medical Association* (June 18, 1921, lxxvi, p. 1721), and also in *Endocrinology* (May, 1921, v,

p. 283) is distinctly in line with the remarks which he made to me. He is clearly a pessimist about organotherapy; he also feels that my interest in the subject and its manifestations are a decided detriment to the profession and to this particular branch of medicine, and that if the blind should lead the blind both will fall into the ditch—although he did not particularly refer to this Biblical simile.

I have great respect for Cushing's surgical acumen. I also have believed in his experiences as reported in his book, referred to above, and have duplicated one or two of them (especially with pituitary therapy) a number of times. If he has changed his mind, *as I believe he has done*, I do not feel justified in changing mine as well. Years ago he helped to convert me to the remarkable possibilities of clinical organotherapy and the fact that he has now "changed his religion" certainly is not going to be sufficient ground for me to apostatize also.

At all events, I am going to quote a number of statements from Cushing's allegorical address in order to direct attention to his present attitude and to draw a conclusion or two therefrom:

"We find ourselves embarked on the fog-bound and poorly-charted sea of endocrinology. It is easy to lose our bearings for we have, most of us, little knowledge of seafaring and only a vague idea of our destination. Our motives are varied. Some unquestionably follow the lure of discovery;

some are earnest colonizers; some have the spirit of missionaries and would spread the gospel; some are attracted merely by the prospect of gain and are running full sail before the trade wind. Traders, adventurers, even pirates are certain to follow on the heels of exploration. In every profession, even ours, are to be found those who gather up beads of information of little intrinsic value which are exchanged for the property of credulous people, as gullible as the natives of a new-found land. Thus do discoveries become exploited and there were discreditable chapters in the histories of all the Great Companies of days gone by. . . .

"To our present short sight it would appear that this sudden enthusiasm to put to sea under the pennant of the ductless glands was largely influenced by the chance discovery in 1909 that certain hitherto uncharted though easily recognizable disorders are due to a state of pituitary insufficiency.

"If this organization [The Association for the Study of Internal Secretions] is to play its proper rôle, it should act as a much-needed stabilizer which, by proper recognition, will enable the profession and the public to distinguish the Cooks from the Pearys of our profession; for though imagination is a desirable quality, in research as well as in exploration, it must be disciplined and, even so, cannot be drawn upon in making out official reports. . . .

"What is more, in many disorders showing a polyglandular participation there is an obvious hypophyseal influence at work, whereas this is far less, if at all, apparent in those maladies which seemingly originate in the thyroid.

"These are but a few of the influences which have led us in such numbers to embark glandward ho! and a good many of us, I fear, have completely lost our bearings in the therapeutic haze eagerly fostered by the many pharmaceutical establishments. For this, however, a credulous profession is largely responsible. . . .

"Never before has there arisen such an opportunity for polypharmaceutical charlatanism. The subject has fired the imagination of the stay-at-homes as did the Mississippi Company and the South Sea Bubble, and there is likely to be the same final crash and then ridicule when common sense begins to breed a proper skepticism. . . . I know of nothing similar unless it was the furore over phrenology.

"The thyroid colony has, in other words, been longest established and though it has been a far cry from Schiff's experimental thyroidectomies in 1856 to Kendall's synthetic production, in 1914, of thyroxin, yet how little do we really know of the background of thyroid disorders, of their relation to the emotions and the sympathetic nervous system, and their pluriglandular interplay.

"With the pituitary gland we are still far behind all this. . . . We must exercise patience and expect even slower progress, for we are dealing with a far more complicated structure and one whose problems evidently cannot be solved without consideration of their relationship to other glands. Of its great importance to the economy, particularly in its influence upon growth and reproduction, . . . there can be little doubt; but these speculative theories are not for the practising physician. He must await the tedious

accumulation of facts which the experimental laboratory and clinic alone can supply.

"It is very easy to say that when the metabolism is low, give thyroid extract, and when high give a counter extract, possibly some lutein. This is a good deal like the hypertension bugaboo, the outcome of the blood-pressure apparatus which encourages the attempt to lower tension if it is too high or to raise it if it is too low. We ought to be beyond this variety of pure symptomatic treatment, for hypertension is not a disease any more than is tachycardia or bradycardia, discussions of which flooded the literature after the introduction of the pulse watch. When our clinical tests get too far in advance of our powers of interpretation, theory is apt to elope with practice. . . .

"The physician or surgeon, meanwhile, even if incapable of participating in these underlying studies, must do the best he can with the mere recognition and classification of clinical types, and should he venture to try glandular therapy, he must be slow to draw conclusions from the apparent effect of glandular extracts given by mouth, particularly when more than one is given at a time. It has been claimed that the body picks out the substance it needs and discards the others, but this has the familiar sound of the gunshot doses of earlier days. The experience with pituitary extract in diabetes insipidus shows that the substance only acts when given hypodermically, and we have very little evidence that other glandular extracts have any action when given by mouth. . . .

"And so, if I may return again to my underlying allegory, if this society wishes to play a useful rôle in furthering advances in endocrinology, it must . . . keep such an exact almanac that

those pursuing the subject in the proper spirit may be able to avoid unfavorable winds, currents and counter currents. It must discountenance the exploitation of the few discoveries which have already been made by those who recklessly under full sail plow through a fog bank of therapeutics, their horns tooting.

"Surely nothing will discredit the subject in which we have a common interest so effectively as pseudoscientific reports which find their way from the medical press into advertising leaflets, where cleverly intermixed with abstracts from researches of actual value the administration of pluriglandular compounds is promiscuously advocated for a multitude of symptoms, real and fictitious. The Lewis Carroll of today would have Alice nibble from a pituitary mushroom in her left hand and a lutein in her right and presto! she is any height desired.

"Endocrinology as a special subject, if it wishes to survive and come to be a factor in medical practice, must look out for the character of its clinical advance agents lest it comes to be utterly discredited. We have nothing as yet, in the treatment of pituitary insufficiency comparable to what Victor Horsley and his pupil Murray accomplished for myxedema, and we are still further behind in the case of the other glands. Indeed, no Magellan or Balboa for ductless gland therapeutics in general has yet appeared, though let us hope he may be on the way. Meanwhile, there is many an imitator of Cortez or Pizarro to trade on the superstitious awe of the natives, who will soon come to be fully disillusioned."

Having read and reread these remarks several

times, I find myself wondering what might have happened if Columbus had not been an explorer—or Cushing had not written his book? It is admitted that there is still much to be attained in the way of accurate knowledge regarding endocrinology and its twin sister organotherapy, and that the idea is indeed “poorly charted,” but to my way of thinking, it is hardly fair to insinuate that those who are attempting to add something to the knowledge along these lines are those who “gather up beads of information of little intrinsic value which are exchanged for the property of credulous people, as gullible as the natives of a new-found land.”

In my conversation with Dr. Cushing he criticized me and some of those interested in the same things that I am, for having too much imagination, and I countered with the suggestion that perhaps he and some of the others had too little. I now recall in his published remarks the following statement: “For though imagination is a desirable quality in research as well as in exploration, it must be disciplined and even so cannot be drawn upon in making our official reports.” And, pray, how is the ordinary doctor to discipline his imagination if he reads Cushing’s book? Perhaps by so doing he has attained an impression that there might be a pituitary basis for certain epileptic manifestations, and then attempts to apply the idea by recourse to organotherapy and finds that

under certain circumstances very considerable benefits accrue. Should he, therefore, acquire the negating attitude of the Christian Scientist who by constant repetition to himself assures himself that "there is no pain", "there is no pain", "there is no pain"? What can he do if, perchance, he may have seen some return for having allowed his imagination to presume that statements such as the following which appear in Cushing's book, "The Pituitary Body and its Disorders", have indeed a scintilla of truth?

"Particularly important is the relationship of convulsive seizures to the states of glandular deficiency. The possibility that an undue excitability of the cerebral cortex may be a consequence of posterior lobe insufficiency is novel to the subject of epileptiform convulsions (p. 272).

"Thus, all told, thirteen patients in the series, with existent hypopituitarism, have shown epileptiform tendencies—a percentage too large to be purely coincidental. . . . Without further observations it would be unwise to lay too great stress on these few experiences, though they are undoubtedly suggestive of a hypophyseal insufficiency. It has been a source of comment by many students of epilepsy that the terminal stage of certain types is often accompanied by an extreme lowering of temperature and slowing of the pulse. Moreover, many of these unfortunates, as is well known, are obese and have ravenous appetites, just as is the case with many of the patients with demonstrable hypopituitarism. We have shown that in some instances there is a high sugar tolerance" (p. 319).

Speaking of the very empirical procedure of pituitary feeding in the treatment of epilepsy, Cushing also says, "Comment has been made also on the amelioration of symptoms in certain cases of epilepsy which were suggestive of hypophyseal origin."

You will note by reading the quotations previously made from Cushing's address that it was impossible for him not to refer to the pluriglandular idea, not merely in critical terms of the work of one who has attempted to popularize its study, and make it readily available by the profession, but in a favorable way, for instance: "We are dealing with a far more complicated structure [referring to the pituitary gland] and one whose problems evidently cannot be solved without consideration of their relationship to other glands"; and later, in a foot note on p. 1724, first column, reporting his series of 255 cases of pituitary disease, 190 of whom were operated, he said:

"Only a few of the 190 surgical cases were acromegalics. The others showed many and varied forms of dyspituitarism. A great number of these patients have been induced subsequently to follow out prolonged courses of glandular treatment. *I cannot say that I have ever seen any definitely beneficial results of so doing except when there has been some concomitant thyroid want indicating the coincidental use of thyroid extract.*" (Italics mine.—H. R. H.)

AND THAT IS JUST THE POINT! I am criticized for daring to presume that when a person

has a pituitary dystrophy sufficiently advanced to show itself clinically, *that there is also a thyroid aspect to it*, and probably that this was present long before signs of either of them were noted. It is for this reason that, in spite of criticism, I prefer to treat functional pituitary dystrophies which are likely to be amenable to organotherapy, with something more than pituitary substance alone, *because I contend that the associated glands invariably are involved also as a system or closely related whole.*

It is a very interesting coincidence that in the same issue of the *Journal A. M. A.* in which Cushing's paper appears (see p. 1795), there is an abstract of an article by Dr. George H. de Schweinitz (originally published in the *Archives of Ophthalmology*, May 1921, i, p. 203) in which the following is stated:

"All patients, therefore, with pituitary body disorder, who also have constitutional syphilis, or from whom the suspicion of such an infection cannot be eliminated, should have the advantage of a full trial of this therapeutic test. In stages of glandular insufficiency the efficacy of organotherapy is probably enhanced by simultaneous administration of mercury (preferably by inunctions) and the gland extracts, even though the presence of syphilis is not demonstrable by the usual methods. DeSchweinitz suggests the probability that a combination of thyroid and pituitary gland extracts is more efficient than either of the extracts alone, and that this combination, associated with

mercury, is more effective than is an extract of one gland, even though given in conjunction with unguentum hydrargyrum."

Now, a word or two in regard to the finale of the Cushing allegory. He says in it: "The experience with pituitary extract in diabetes insipidus shows that the substance only acts when given hypodermically, and we have very little evidence that other glandular extracts have any action when given by mouth." This is Cushing's complete sentence; but I think it is most incomplete, for he should have added, "when given by mouth *in diabetes insipidus*." Other glandular extracts have a therapeutic action when administered orally; furthermore, the foregoing statement is contrary to many of Cushing's statements in his own book, which it would appear he is now repudiating.

It may be possible that some of the failures with pituitary therapy by Cushing and others, in cases which it was hoped would be responsive to such treatment, *were due to the fact that the associated conditions were ignored*, for it is absolutely certain that many a failure with monoglandular therapy has been chalked up against endocrinology as a whole when failure might have been turned into success had the treatment been pluriglandular, or exactly as Cushing says:

"I cannot say that I have ever seen any defi-

nitely beneficial results of so doing [prolonged pituitary therapy] except when there has been some concomitant thyroid want indicating the co-incidental use of thyroid extract."

It is obvious that there are two sides to this question. Cushing has expressed himself to many as a pessimist. I prefer to be an optimist. He tries to poke fun at the pluriglandular idea by imagining a dystrophic Alice in an endocrine Wonderland, "nibbling from a pituitary mushroom in her left hand and a lutein one in her right and presto! she is any height desired." In our efforts to further a practical interest in pluriglandular therapy we do not suggest "nibbling" any kind of endocrine mushroom and, unfortunately, there is no "presto" about it, for any results from organotherapy only come after persistent and prolonged treatment. And the mariner in this uncharted sea who is not willing to "plow through a fog bank of therapeutics," as Cushing puts it, *will never get to the other side of the ocean and the land of promise never will be discovered.*

VII

"THE ENDOCRINE GLANDS—A CAUTION"

"Be thou chaste as ice, as pure as snow, thou shalt not escape calumny."—Shakespeare.

THE belittlement of pluriglandular therapy has attained considerable proportions during the past year, and as the enthusiasm engendered by the clinical results of this method grows, so do those, who previously have said, "It can't be done", shout the louder in their derision. Without exception agitation has always been rife against advances in any field. But there is at least some consolation in the fact that "things true and evident must of necessity be recognized by those who contradict them," as Epictetus said a good many hundred years ago. A friend of mine recently said to me: "You should be encouraged because you and your work are worthy of the damnation given to you."

Further evidence of this opposition is found in the leading editorial in the issue of *The Journal of the American Medical Association* (May 28, 1921, lxxvi, p. 1500). This editorial which carries the title used to head this chapter, is worthy of comment because it directs attention to several points which I have been attempting to emphasize for several years, even though the editor's views differ decidedly from my own. By reprinting this editorial, I am availing myself of the opportunity

to interline several pertinent remarks which I believe are decidedly to the point.

I am perfectly willing to admit that there is still much to be learned in regard to the internal secretions. From the clinical experience which I have personally had, and from many things which have been told me by many physicians, I am confident that I am on the right track. Mistakes are not improbable, but these are always part and parcel of the human make-up; possibly others may err occasionally!

A generous number—several thousands—of reputable practicing physicians have seen fit to speak kindly of my efforts. Have their experiences been developed upon a foundation wobbly from corroding untruths? Have they been the victims of exploitation? Have they been unduly credulous? Have they come to their knowledge as a result of accident?

The reason for the great developments along these lines, is that *we are right in our premises* that the endocrine glands indeed deserve consideration much more often than the profession previously has been in the habit of giving them. Furthermore, these organs *should be studied together*, rather than as has been the custom for many years, from the clinical standpoint of the most obviously affected organ. If this is correct, then pluriglandular therapy should be a great advance over the older monoglandular method, as,

indeed, it is. The whole method has exceptional value, because often such organotherapeutic procedures are as valuable as a diagnostic means as they are for their prospective therapeutic help.

The following is the entire editorial from the *Journal A. M. A.*, with some comments as they occurred to me, and as published originally in the July, 1921, issue of our little house-organ, *The Organotherapeutic Review*.

"The bearded lady, the giant, the fat boy, and the midget—those 'marvelous freaks of nature' of the dime-museum days—we have learned to regard as the victims of disordered endocrine glands. So profound are the effects which these remarkable organs can produce in the body, upsetting such essential processes as sexual development, growth and metabolism, that the imagination of both laboratory worker and clinician has been greatly stimulated." [*And, fortunately, the results of a good many of these dreams have been made available to ordinary doctors and the clinical experiences that they have come to depend upon from the application of some of these materialized dreams have stimulated a good deal more than their imaginations!*] "No wonder that hopes have been stirred that these processes may be placed under control, that old mysteries of disease will be explained, and that hitherto hopeless cases can soon be satisfactorily treated. Unfortunately, we are still deeply ignorant of many important aspects of endocrinology." [*While this is all too true, it is getting a bit monotonous to hear so continually "we still know very little about this," "the fathomless depths of this science," or "our*

deep ignorance." Believe me or not, as you wish, we are much more intelligent about the endocrines and organotherapy today than we would have been had we conceded the depth of our ignorance and given up our clinical work along these lines as some seem to have done.]

"The conditions in the body which control the glands of internal secretion are still almost wholly unknown. There is evidence that the suprarenal medulla and the thyroid are subject to sympathetic stimulation, but what of the others?" [Undoubtedly those chemical and nervous factors which stimulate the adrenals or thyroid are such that they influence other tissues—endocrine or otherwise—and their cells are not so indifferent to these subtle factors that they are immune to hormonal influences.] "The glands are probably complexly interrelated, but in only few cases has satisfactory proof of mutual influence among them been demonstrated." [I am glad the word "probably" was slipped in here. If this editorialist had left it out entirely he would have been telling the unadulterated truth—for there is no whit of a probability about the interrelationship of the ductless glands. We may not understand why these interrelationships exist, nor may we have learned all that there is to know about their extent, but I do differ most emphatically with this writer as to "the satisfactory proof of mutual influence among them," even though he indeed admits that this relationship has been proved in "a few cases." I do not think I am overstating by saying that I could quote a round hundred articles or abstracts emphasizing the pluriglandular aspects of endocrinology from the Journal A. M. A. itself.]

"Though we glibly talk of 'hormones,' only two

endocrine products are known chemically, thyroxin and epinephrin, and there are physiologists who do not concede a hormone function to epinephrin." [*The editor overlooks Brailsford Robertson's work with tethelin at the University of California, or the references to hypophysin sulphate, a chemical, by H.Fühner, possibly because the latter is German. As a matter of fact, hormones do not have to be chemically isolated to be therapeutically efficacious, else more than twenty-five years' experience with thyroid therapy is nullified, or thousands of clinical experiences with ovarian products are put into the editorial limbo.*] "The nature of the supposed active agents of most of the glands, e. g., the ovary, the corpus luteum, the suprarenal cortex, the anterior pituitary, the parathyroids, the thymus, and the endocrine cells of the pancreas, has not been determined. Nor has it been demonstrated that most of these organs contribute any specific internal secretion." [*The editor seems to be reverting to the attitude of those who deny realities because they are unable to regulate control of them, or of the ignorant individual who belittles a thing because he is ignorant about it. There is absolutely no need to demonstrate that "most of these organs contribute any specific internal secretion." We are satisfied to presume it if our presumption will enable us to get anywhere in our treatment of disease.*] "They may, conceivably, exert their influence by removing toxic substances from the blood stream and metabolizing them to inert forms. Epinephrin, the nature of which is understood [*though the editor has just stated that even yet some "do not concede a hormone function to epinephrin*], is known to disintegrate rapidly in an alkaline me-

dium, and, though highly potent in many directions when injected intravenously or subcutaneously, is without physiologic effect when taken by mouth." [*Here the editor forgets, wilfully or ignorantly, several published clinical reports as well as an article of my own—"The Oral Administration of Adrenalin," New York Medical Journal, November 4, 1916—in which, after bringing report after report to confirm this opinion, I dared to invite such armchair critics to "swallow just one bottle of 1:1000 adrenalin chloride solution, for it contains only about 1/2 a grain of the real active principle."*]

"Until we learn more about the character of the essential elements of the ductless glands and their precise effects, we cannot be sure that they also are not altered or destroyed in the alimentary canal." [*But why should we stop our successful clinical experiences with oral organotherapy while our ultra scientific friends "learn more about . . . their precise effects?"*] "And to what degree is substitution therapy possible? Its value has been proved in thyroid deficiency, but it is useless in pancreatic diabetes." [*Not so, if R. Lépine of Lyons, J. H. Pratt of Boston, W. M. Crofton of Dublin, G. Zuelzer of Berlin, and many others are to be believed. Mind you, the word "useless" is very explicit; and by making reference to the reports of the above clinicians, I do not say that the Langerhansian principle is as comparatively valuable as the thyroid principle in corresponding circumstances, but I do deny that "substitution therapy is useless in pancreatic diabetes."*] "Too often organotherapy is justified by the patient's 'feeling better,' or by the disappearance of subjective symptoms—criteria of every uncertain

quality." [*Here are the same old arguments again—akin to those of the Eddyite—"might have happened anyway," "probably due to suggestion," "no telling how much of the presumed benefit was coincidental," and so on. I wish the editor would change chairs with me and read my letters for just one week!*]

"The normal rôle of the endocrine factors in the organism is largely unknown. Much of the general opinion is based on faulty inference." [*What criteria determine whether your judgment is faulty or mine? Maybe it is wrong to infer altogether. Anyway, I prefer to leave it to the patients—they know, they believe in you, they tell their neighbors about your work, they don't give a continental for anybody's inferences—faulty or scientific. What they want is results and they get it many more times when their physician thinks for himself and is willing to give them the benefit of a known-to-be effective measure.*]

"Injected epinephrin raises blood-pressure. The inferences have been drawn, therefore, that the suprarenal medulla is essential to the maintenance of normal blood-pressure, and that hypotension means 'hypo-adrenalism,' and hypertension 'hyperadrenalism.' No conclusive evidence exists to support these inferences; indeed, there is excellent evidence that the suprarenal medulla has nothing to do with maintaining the natural blood-pressure level." [*Believe it or not, as you wish. I have as much right to believe that the adrenals are a part of the pressor mechanism as you have to think otherwise. If Cannon is wrong, if Sergent has been fooled ever since 1898, and if Sajous, Carnot and scores of others are mistaken, then I prefer to be with the "few" who disagree with such self-*

constituted authorities whose clinical inexperience is so obvious.] "The idea that the posterior lobe of the pituitary is active in labor and in lactation is based on the same fallacy of assuming that the pharmacodynamic action of a powerful drug indicates the physiologic rôle of the organ from which it is derived." [Not by any means. Fortunately, my skirts are clear in this respect, for I have repeatedly called attention to the fallacy of believing that a woman in labor was suffering from the insufficiency of the posterior lobe of the pituitary gland, because an injection of liquor hypophysis stimulated the inert uterine muscles and precipitated the much desired event.] "Again, there is no satisfactory clinical test for any assumed internal secretion, as such."

"Altered metabolism in thyroid disorders permits a certain amount of insight into the type of disturbance present. And, of course, when conditions are extreme, fairly definite inferences can be drawn in such diseases as acromegaly and myxedema. Minor clinical changes, however—headaches, flushes, unstable blood-pressure—are commonly attributed to endocrine disorders on no definite evidence whatever, often on the basis of the therapeutic fallacy mentioned above. The facts should be faced that much of endocrine physiology is in a state of chaos, and that selection of bits from this chaos to bolster up clinical theories is sheer futility." [Of course a "scientific" gynecologist cannot possibly be persuaded to believe that the headaches, flushes, and unstable blood-pressure related to the menopause are in any way connected with the removal of an endocrine factor to which the body has been accustomed for thirty years or more. Undoubtedly the

experiences resulting from the clinical application of these unscientific methods of organotherapy are merely coincidence. I think, however, that I have had enough personal experience to deny flatly that "minor clinical changes such as headaches, flushes, and unstable blood-pressure are commonly attributed to endocrine disorders on no definite evidence," on the very best of clinical premises—the fact that the endocrine or organotherapeutic regulation of the real or fancied dyscrinism causes a mitigation or removal of the headaches, flushes, and pressor vagaries. Again it is the patient that decides—not the editor!]

"Confronting our real ignorance of many important features of endocrinology are positive statements of facts when the facts have not been established, large assumptions of assurance when there is no clear certainty, and a formulating of laws for diagnosis and treatment when no respectable basis for either exists. Illustrations of these charges can be found on all sides in books and articles and, especially, in widely scattered advertising matter." [I have been expecting it for nearly two columns. It had to come, for here, doubtless, is the text for this long hypercriticism, and all of this stuff purporting to deny our statements and decry our work invariably includes a "slam" of this type, in order to be true to form! Suppose I happen to be mistaken about my own relation to this—I am having a lot of fun in what we are doing here; the results we are getting satisfy me and my customers and their patients often enough to make it thoroughly worth while. What do I care whether the facts have been established to the scribe's satisfaction, or not, so long as we are getting real results every day? IT IS

ACHIEVEMENT THAT DETERMINES THE WORTH OF ANY METHOD OR THEORY. *Further, I should be glad to see as much proof on the part of the critic as I can muster up against him. What are the "positive statements of facts" that "have not been established?" That adrenalin "is without physiological effect when taken by mouth?" That "the adrenal medulla has nothing to do with maintaining the natural blood-pressure level?" Or that "minor clinical changes—headaches, flushes, unstable blood-pressure—are commonly attributed to endocrine disorders on no definite evidence whatever?" If so, have I not as much right to deny the conclusions of the editor of The Journal of the American Medical Association as he has to class me with the prevaricators and the charlatans?]*

"Credulity, under these circumstances, has evil consequences. It helps to fix a sense of security, a sense of being satisfactorily informed, when there is little, if any, justification." [Too bad! *Here I have been hoping that we were learning something; that we were really beginning to get somewhere, and now suddenly we are thrust back into the endocrine Stone Age and have to find some incontrovertible facts, the incontrovertibility of which is acceptable to the editor or printer's devil who wrote this statement. The encouraging remarks of visitors to The Harrower Laboratory, the numerous unsolicited letters of commendation from physicians, and even the statements of patients themselves whom we are so fortunate as to meet personally—all seemingly must be classed with "mortal error." How credulous we have been!]* "It hinders medical progress by substituting simple faith and enthusiasm for the care-

ful, critical study that is sorely needed. It opens the door for exploitation of the medical profession by charlatans and quacks and unscrupulous manufacturers. [*Sic!*] Medicine is humiliated rather than served when we swarm with the crowd after the latest therapeutic fad, accepting as gospel every claim that is made, if only it is made with sufficient positiveness." [*Not so, only if such claim makes good clinically after we have been reasoned with, converted sufficiently to make the effort, and, finally, have been satisfied at the unusual results that frequently are secured.*]

"We appeal, however, not for general condemnation of endocrinology, as a subject of interest, but for a proper scientific attitude toward the data that are advanced." [*What is the proper definition of the word "proper" in the proper kind of dictionaries?*] "Quite as numerous, perhaps, as the group that throngs heedlessly after each new interest is the group that will have none of it, good, bad or indifferent." [*As represented by a certain editorial writer for The Journal of the American Medical Association, issue of May 28, 1921, page 1501.*] "This is merely throwing out the baby with the bath. Although less vociferous than the impressionistic school, there are groups of clinical and laboratory investigators who are bending their best efforts toward the solution of the numerous and baffling problems that the field presents. The efforts of these men are deserving of the whole-hearted support of their colleagues." [*But those who dare to differ with "authority" may be damned!*] "To the well-trained clinician, the existing chaos in this field may well stand as a challenge to his constructive attention. Interest in the ductless glands was initiated by clinical

study." [*And will be developed by persistent clinical study—not by armchair philosophy.*] "Addison, Oliver, Parry, Graves, Kocher, Lancereaux, Marie—the names of these clinicians mark the steps of our progress." [*The writer probably and with purpose has left out the names of the great materializers of knowledge along these lines—the men who have made practical the fundamental suggestions of those mentioned in the illustrious list just named. I refer to Elliott of London, Sajous of Philadelphia, Carnot and Sergeant of Paris, Lorand of Carlsbad, Cushing of Boston, Engelbach of St. Louis, and others whose names I need not mention.*] "But these men helped to advance medical knowledge by careful study of their cases, by correlation of similar conditions, by cautious and limited inferences." [*What is the proper definition of the word cautious?*] Is it, "*Be sure you're right, then go ahead,*" or is it, "*Be sure that the other fellow has some good reasons behind his remarks, and then proceed to prove or disprove them?*"] "The clinic still provides disturbances, probably endocrine in origin, [*not absolutely but only "probably"*—that the laboratory cannot duplicate. [*And it also provides a kind and amount of truth that the laboratory cannot duplicate, either.*] "The opportunity to contribute to professional knowledge in this field is still great. The situation calls not for the gullible enthusiast but for the critical clinical investigator, not for a stampede but for cautious progress. And so far as the well-tried methods of careful observation, careful record, careful test, and careful inference are employed, they may reasonably be expected to yield useful information."

VIII

THE PANCREATIN MYSTERY

"Assertion does not become proof by mere reiteration—a statement of opinion is as nothing when compared with a report of experience."

SOME years ago there appeared in *The Journal of the American Medical Association*, under the heading "Propaganda for Reform," some comments sponsored by the Council on Pharmacy and Chemistry of the American Medical Association regarding the therapeutic efficacy of pancreatin.

I refer to this particularly because while pancreatin is used clinically chiefly for its tryptic ferment value it is none the less an organotherapeutic product, and the conclusions drawn were quite at variance with the truth.

This past history is revived here to illustrate the fallibility of human judgment and to call attention to the grace with which criticism is accepted when it is inevitable, and also to point out the lack of apologies in cases where wrong has predominated and right has been thoroughly neglected.

For many years tablets consisting of pepsin, pancreatin and certain other remedies—carminatives, charcoal, etc.—have been put out by leading pharmaceutical houses and many millions of them have been used by many thousands of physicians. In fact, several years ago when I was talking about this with a certain manufacturer of

digestive ferments he referred to a contract that his firm had with a manufacturer which involved about \$25,000.00 worth of pancreatin per annum, and I could not help remarking, "It is funny how so much of this stuff is used right along and yet the profession does not get the idea of the Council that pancreatin by mouth is useless!"

Memory is an excellent adjunct in writing and I remember a number of statements of no mean importance which have a decided bearing on "the pancreatin mystery."

In 1907 and again in 1915 the Council on Pharmacy and Chemistry of the American Medical Association had a good deal to say regarding this matter and in a critique of lactopeptin they committed themselves quite definitely in regard to their opinion of the therapeutic value of pancreatin given by mouth.

In an editorial in *The Journal A. M. A.* (October 23, 1915, lxxv, p. 1466) entitled "A Therapeutic Absurdity", in referring to this preparation they say that lactopeptin is supposed to contain . . . pepsin and pancreatin "and this, in the light of present-day knowledge, brands these products as therapeutic absurdities." The statement is then made that

"it is axiomatic that pepsin and pancreatin are never indicated at one and the same time and it is practically impossible for the two substances to act together."

Later on, a preparation of this kind is again called "an indefensible therapeutic and pharmacologic absurdity." In the same issue of *The Journal*, under the subheading "Propaganda for Reform" (p. 1477) there appears the following statement:

"Mixtures of pepsin and pancreatin are therapeutically irrational . . . under pharmacologic conditions such mixtures are chemically impossible. . . . As stated at the outset, whatever the tryptic activity of the mixture (lactopeptin) it is therapeutically useless. A demonstration of tryptic activity in a mixture containing both pepsin and pancreatin is of merely theoretical interest."

Further on in the Council's actual report we read the following:

"It is a commercial impossibility to make mixtures of pepsin, pancreatin and lactic acid so that they can display any material tryptic activity."

"It should be reaffirmed that mixtures combining peptic and pancreatic activities are not feasible, because pepsin cannot act except in the presence of acid, and pancreatin is destroyed by acid and by peptic activity. . . . Theoretically, as well as practically, however, pepsin and pancreatin cannot exist together in solution."

Incidentally, these final statements—not hints, not suggestions, but positive and unqualified remarks: "Pancreatin is destroyed by acid and by peptic activity"—are based upon laboratory experiments for tryptic activity by several investi-

gators, who, by the way, had arrived at quite different conclusions. The final remark in the secretary's summary is that

"even if tryptic activity were conceded, the preparation, like all preparations containing pepsin and pancreatin, would still be, as previously stated, therapeutically irrational."

The evidence seems to show that *liquid* preparations of this type, especially those containing acid, are not stable, and even this is open to question; but since the use of pancreatin is far more common *in dry form* the criticism above is not well taken.

In another item, published some months later in the same journal (December 11, 1915, lxxv, p. 2108), appears the unsigned statement: "It is doubtful if the pancreatin used in this mixture could ever enter into a digestive process in the intestine." Note that there is now an element of doubt!

There seems to be no possible chance of misunderstanding these statements. Not merely are these "authorities" sure that pancreatin is destroyed in the stomach and consequently ineffective as a remedy under these circumstances, but they are impugning the honesty and integrity of those who have been "foisting them upon the profession."

But here is another side to this history. Prof. J. H. Long, in charge of the Department of

Physiological Chemistry in the Northwestern University, and his associate, Doctor Mary Hull, published several papers in the *Journal of the American Chemical Society* and in *Science*, to which reference will be made here. The first of these is a paper by said authors entitled "On the Assumed Destruction of Trypsin by Pepsin and Acid" (*J. Am. Chem. Soc.*, 1916, xxxviii, p. 1620) which is the report of a comprehensive series of researches done with the assistance of a grant from the American Medical Association and in an attempt to assist the Council to come to some conclusions—after they apparently already had reached their hard-and-fast conclusions!

At the beginning of this paper the writers state that they were attempting to determine whether pancreatin was destroyed in the stomach and whether the administration of pancreatin by mouth was a therapeutically active procedure.

The conclusions of a large series of carefully worked-out experiments in individuals as well as animals are of special interest:

"If sufficient protein is likewise present, the acid, in combining with it, is unable to destroy in the same degree. When the acid concentration is reduced in this manner . . . tryptic activity persists, even though several hours at the temperature of the body. This is a practical condition which very commonly obtains in the human stomach. An active tryptic ferment would unquestionably pass with the chyme . . . into the duodenum . . . and there be able to pro-

duce a normal proteolytic digestion of some degree."

And later, in a second paper on the same subject, referring especially to observations in animals (*J. Am. Chem. Soc.*, 1917, xxxix, p. 162) these writers conclude further:

"In all the animals the secretion of pepsin and acid was abundant, and from this point of view the conditions for the persistence of trypsin were not favorable. Yet, in the larger number of the experiments, this latter ferment was not destroyed by the other combination where sufficient protein was present to bring the concentration of the free acid down to a certain value. Trypsin seemed to be destroyed or greatly weakened only when the acid was in excess with pepsin."

To state the matter simply, the statements of the Council on Pharmacy and Chemistry were disproved as the result of experimental work made by a capable man, of their own selection and at their own expense. As yet I have not read of any apologies to the New York Pharmaceutical Company, the makers of lactopeptin, nor have I seen any extensive retractions in *The Journal* in regard to their position.

The moral to be drawn from the above recital of facts is that so-called "authority" is not always characterized by impeccable truth, and that when the clinic indicates the feasibility of a measure—pancreatin has been given successfully these many years by mouth and its oral administration still

continues to be a remedial procedure—in all probability it is likely to be in close proximity to what is right even though exact explanations are not forthcoming.

What has just been said reminds me of still another instance of the fallibility of “authority” which may be reported here to substantiate my previous remarks in this chapter. There is a book published some years ago by the American Medical Association entitled “Useful Drugs” which is intended to serve as a *vade mecum* to physicians and students. It is supposed to be authoritative, yet I note that so common a remedy as cod liver oil is held up to question as a therapeutic agent by the suggestion that its value as a remedy depends probably entirely upon its nutritive properties. It has been used as a real nutrition-influencing remedy—not merely as a food—for more than a hundred years; but just because the authors of this compendium did not know just how the smelly stuff could serve as a remedy, gave no warrant for their criticism in the face of the accumulation, during scores of years, of clinical evidence of its therapeutic—not dietetic—value.

More recently, however, in another publication from the very same office—*The Journal of the American Medical Association*—we find the recently disclosed reason for the empirical clinical conclusions of thousands of physicians for 100

years! A certain Doctor Hess (Newer Aspects of Some Nutritional Disorders, *Jour. A. M. A.*, March 12, 1921, lxxvi, p. 693) emphasizes the well-known facts regarding the value of cod liver oil in the cure of rickets and makes the assertion that this disease could be practically abolished in New York City for the paltry sum of \$100,000.00 a year—figuring the cod liver oil at its current price. Reference is also made to the researches of Zilva and Miura at the Lister Institute in London, which showed that crude cod liver oil may be 250 times as rich in the vitamine-A, as butter.

In other words, vital therapeutic results of unquestionable character now known *to be due to vitamines*, but not attributable to them through ignorance of their character at that time, were decried or belittled in the book "Useful Drugs."

Might not these same "authorities" be mistaken regarding some other matters, and misled by their technical advisers?

IX

A PATHOLOGIST'S PECULIAR VIEWPOINT

"Censure is the tax a man pays to the public for being eminent."—Dean Swift.

Johns Hopkins University is an institution out of which nothing but truth should come—it ought not to be otherwise. In its very laudable effort to add to the world's supply of knowledge the faculty of this institution recently instituted a series of medical lectures by members of its staff, to which the medical profession and the public are invited.

The first of these lectures was given in Baltimore by Dr. William G. MacCallum, Baxley Professor of Pathology at Johns Hopkins University, on April 6th, 1922. According to the newspaper report before me, "The Cult of the Monkey Gland" may have been the title, and in the course of his remarks the speaker harpooned with ridicule the claims of those who have believed in this idea.

I have had a few things to say about the monkey gland craze and have compared it with what followed the well-intentioned and carefully-worked-out reports of Brown-Séquard in 1889. The effect of Brown-Séquard's work, and for that matter the whole procedure of organotherapy, was set back many years by the charlatans of Paris who saw in the announcement a chance to

separate their especially susceptible patients from still more money. I believe that the same kind of "black eye" has been given to the well-intentioned efforts of many an endocrinologist because of a good deal of unwarranted notoriety about the monkey gland idea. (Parenthetically, monkey glands contain no more therapeutic virtue than any other kind of animal glands, and neither do goat glands.)

Professor MacCallum did not limit his remarks to a consideration of Voronoff and other transplantation enthusiasts, but attacked pluriglandular therapy very vigorously: it was clear that he considered my work in exactly the same light. Early in his remarks he explained that if he could succeed in injecting a certain degree of skepticism into his hearers he would have succeeded at least partially in his effort. He referred to certain manufacturers who "were exploiting organotherapy for personal profit" and told of "a regular flood of literature which is going through the mails daily, some of which has just come to me this morning." He remarked that some of these people even "had written whole books on the subject" which he felt had been done "under the influence of autohypnotism."

He then made some interesting statements which are accepted by the majority of the profession in regard to the remarkable usefulness and clinical availability of thyroid preparations, but

went on to state his belief that so far as there being any therapeutic advantages in the use of adrenal, orchic or ovarian therapy, it was "all bunk."

I have before me a full report of this meeting and a clipping from a Baltimore newspaper which came out the next morning. It was clear that Professor MacCallum not only was conservative, but as the newspaper reporter states, "he was more than skeptical, he was scornful" of certain attempts that are being made to materialize the good to be found in various phases of glandular therapy. Near the close of his remarks he produced from his pocket some literature and letters which came from The Harrower Laboratory, and from the latter read "Why not prescribe Antero-Pituitary Co. and give the patient the benefit of the doubt?" and added some comments perfectly in harmony with his previous statements.

I am willing to admit that the theory of cellular rejuvenation advanced by Voronoff and others does not appeal to me; and I am also glad to give MacCallum credit for a greater degree of intelligence regarding the internal secretions than some of his colleagues apparently have, for about ten years ago MacCallum published some very interesting reports of his work in New York City regarding the parathyroid glands and calcium metabolism. He is one of the men who really have added something to endocrinology. But because

a man has attained a position of eminence in his line does not make him an authority in all other lines, and while MacCallum's word may be valuable regarding matters with which he is acquainted—pathology, for example—I am not at one with him as regards his remarks about pluri-glandular therapy; first, because apparently it is not in his line; and, second, because it was clearly evident during this lecture that the speaker was not intelligent on the subject. As a matter of fact, he referred to Adreno-Spermin Co., a product of The Harrower Laboratory regarding which he had received some literature which he flourished before his hearers, and stated in so many words that he did not know what the preparation contained, but in the same breath gave the impression that he thought it had six or seven different ingredients, which happens not to be the case for there are three glandular ingredients—thyroid, adrenal and spermin—and a useful adjuvant excipient.

It is within the bounds of possibility that even Professor MacCallum is a victim of the same variety of autohypnotism which he suggests has influenced me or others. Autohypnotism spares neither the high nor the low.

At all events, the scorn of Professor MacCallum, like pepper, served to "bring out the flavor" in the minds of several Baltimore friends from whom I already have heard in somewhat satirical strain.

A question which is pertinent and which always occurs to one when "commercialism" is flung in one's teeth is this—why all this "fuss" about commercialism, why this utter deprecation of it, when it is a fact that all of us are "commercial" enough to see that we make a living, and a "good" living at that. There may be a few individuals who are so opposed to commercialism that they refuse to work and would rather be supported by their friends; but who would want to be classed with them? Who would want to wear their laurels? I think even though Professor MacCallum is "wedded" to science—and my regard for him as a scientific man is above the ordinary,—he too, would consider it a stricture on his ability to be accused of being above making a living. He also wants the just returns for his labors and I suspect that he also thinks highly of his labors—believes in them despite what others may say. If this is not the case always, the man who seeks fame and fortune soon deteriorates into something not worth while, and I am sure Professor MacCallum would not want me to do this, just as I would not want him to do it.

The letter to which Professor MacCallum refers was sent out from Glendale at a time when it would be likely to reach all the physicians in Baltimore early in April. This is not a confession on my part or a boast—it is merely the statement of a fact of which I need not be ashamed. To

prove that I consider this letter only in the light of an act that carries with it no regret, I am re-printing it here:

My dear Doctor:

Give the epileptic "the benefit of the doubt"—for, of course, there is some doubt—is the fair way to recommend Antero-Pituitary Co. (Harrower) in the treatment of this strange disease.

While epilepsy is not always of endocrine origin, many times there is a large endocrine aspect, especially in children. Organotherapy has cured epilepsy *entirely*. In other cases it has changed its character, and in still others has increased the intervals between the attacks—for example, from 25 a day to 1 a week!

This pluriglandular formula, anterior pituitary in generous dosage, thymus, and a small dose of thyroid, originally was and still is used in developmental defects in children. It has accomplished wonders. Its use in epilepsy came from noting frequent benefit in epilepsy accompanying backwardness of endocrine origin.

A physician in Georgia refers to this treatment in the following words: "Regarding Mrs. Y., whose history I gave you some months ago, I am glad to report that she has had no more 'grand mal' attacks since the end of the first week's treatment with Antero-Pituitary Co., and no return whatever of the seizures. Her temper and general disposition have improved greatly, and she is less nervous and more normal than for many years past. *Mirabile dictu!*"

The following comes from a physician in Montreal: "This is the third hundred I have ordered for patient with epilepsy (grand mal and petit mal) fifteen years standing. Result: He has never felt so well for years—no attacks since starting treatment."

Another physician in Brooklyn, N. Y., in referring to his experiences with my products writes: "The first case of epilepsy about whom I wrote you will pass the year mark this month without a single attack."

Since the prospects in epilepsy are poor, and bromides really do not get us anywhere, *why not give some of these patients the benefit of the doubt?* The enclosed booklet gives one or two more points, and I will gladly send on approval a copy of *Harrower's Monographs on the Internal Secretions*, the third 92-page issue of which is devoted to "Epilepsy: An Endocrine Disorder," and contains a consideration of the literature establishing this position.

From my own personal point of view, I cannot see anything deserving of scorn in an attitude of this kind, nor do I see anything reprehensible in attempting to broaden our knowledge in a particular field which happens to interest me especially. There are more ways than one of learning something worth while, even though opinions may differ about them.

X

"PROPERLY SUPERVISED CONTROLS"

"He who seizes the right moment is the right man."—Confucius.

EVERY so often a cultured medical writer, usually connected with one of the more or less important institutions of learning, makes some remark about a published statement by a colleague indicating that he does not agree with it, and from his superior position he looks down upon his fellow member and insists that clinical deductions are of no value unless they have been made under circumstances agreeable to him. "Properly supervised controls" are essential and without them clinical observations can have little dependability or value. Hence the "ordinary doctor" can have no facilities for passing correct judgment upon matters of clinical importance because of the limitations of his professional circumstances.

The only way to establish a therapeutic procedure would be "to get it tried out in some of the large hospitals," as one critic expresses himself. None but the leading men have the necessary intelligence to draw clinical deductions and the work of investigation necessarily must be done in a hospital—and preferably a "large hospital".

There is a very obvious and unfortunate tendency in medicine to make invidious comparisons. On the other hand, it is admittedly a difficult thing

to pass judgment on the reports obtained from a series of physicians working under widely varying circumstances and, as one physician, who already has been quoted in the Introduction, says: "It is very easy to get a statement from some crossroads doctor to the effect that he has gotten wonderful results with this thing or that, but such reports do not mean anything." I agree, but only, however, if such reports are rare or occasional.

In conversation with a prominent medical teacher the other day he said to me that he believed there was a tendency to mass action on the part of the medical profession—that their enthusiasm for new things was wave-like and that they "believed anything they were told." This particular authority in discussing some of my own work tried to make me believe that the reports given to me and upon which I am basing my opinions and statements were not based on proper criteria, and that these doctors were being fired by some of the sparks of the enthusiasm with which I am carrying on my own work.

Either clinical reports are valuable or they are not. We must either believe or disbelieve; and I, and many thousands of other physicians, have chosen to believe certain things regarding the internal secretions and especially that there are decided advantages in pluriglandular therapy in the treatment of quite a wide range of functional

disorders, and that the numerous reports gathered from so many sources—even, occasionally, from the crossroads—constitute a true indicator of the inherent value of the method and the remedies based thereon.

It has always been my rule in my study of the literature on this subject, when I encountered some point of prospective value which at that time was new to me, to attempt to find corroborative evidence in the writings of others—it is surprising very often how a seemingly “new” thing is not new at all but has been written about many times previously—and also when I have had clinical opportunity I have attempted to reproduce clinical experiences similar to those of which I have recently read. This procedure is exactly what any responsible and progressive physician would follow who has no other opportunity to verify every single thing that he hears or reads. Somebody refers to something that has happened and when an opportunity to repeat the experience presents itself, he does his best—he is an empiricist, if you will. Soon he develops opinions of his own based upon experience and comes to know, and knows that he knows!

If an unbiased physician applies a presumably reasonable remedy in a number of instances the results obtained soon convince him of the reality of its value as well as of the reasonableness of the remarks which may have prompted his original

interest in the procedure. Such clinical experiences, to my way of thinking at least, are worth a very great deal more to the physician himself than all of the written and spoken statements of another, simply because "the other fellow is not treating your patients, and you are responsible to your patients and to no other."

Now it is perfectly true that there should be some discounting of all sorts of clinical reports, for both the temperament and judgment of various physicians do not follow certain standards; but to say that all clinical experiences that are worth anything must be in the work of a certain limited class of men with specially fine facilities, does not agree with my own opinion and I have not hesitated to say so despite the fact that it has brought down upon me the criticism (see *Journal A. M. A.*, Nov. 5, 1921, lxxvii, p. 1499), that "scientific medicine is systematically belittled as unpractical" in my publications. I think it depends a great deal on what is understood by "scientific medicine".

It must be remembered that the impressions that I have gained about the internal secretions and pluriglandular therapy, and which I have succeeded in combining into the tangible and valuable remedies produced in The Harrower Laboratory, were secured from the statements of other clinicians who certainly were intelligent enough to make reasonable reports. Much of this work has

been done abroad, and I firmly believe that the conclusions of these foreign physicians are just as dependable as the conclusions of any physicians here. In fact, this subject of organotherapy and the internal secretions has been given far more consideration and is better understood in France, Italy and England than it is in the United States, and most of the really great advances along this line have originated abroad, although in the last decade or so I will admit that American investigators have added materially to the sum of knowledge along these lines.

The idea of "properly supervised controls" has become a shibboleth which is being quite seriously overworked by some physicians who desire to belittle certain clinical reports about organotherapy and especially pluriglandular therapy. For instance, the possibilities of organotherapy in the treatment of epilepsy were developed upon clinical experience, and I think I can very properly mention here how I became enthusiastically interested in this matter.

Organotherapy is an accepted measure in the treatment of developmentally defective children, and knowing that no cretin, mongol or less seriously affected child was suffering solely from a thyroid insufficiency, and presuming very properly that certain of the other glands also must be involved, I devised a pluriglandular formula—Antero-Pituitary Co. (Harrower) for the treat-

ment of the large hypoplastic class which MacCready calls "children requiring special attention." Its use certainly has broadened the organotherapy of such cases very wonderfully and made possible results that previously had not been secured with long periods of thyroid therapy alone, even though this was definitely indicated and obviously valuable. Now it happens that epilepsy is not uncommon in this particular class of children, and it was not long before a number of developmentally defective children *who also had epilepsy* had been given the benefit of this pluriglandular formula.

In the course of time a number of clinical experiences supplementing my own were reported to me from various physicians, indicating that not merely had there been benefit from the standpoint of growth, development, mentality, walking, talking, etc., *but that in some of the cases the epilepsy apparently had been cured*; whereas, in other cases with many attacks a day, the seizures were reduced to one a week or to still longer intervals. Very soon it was clear that this was more than a coincidence, and I began to study the possibilities of the endocrines in relation to epilepsy and discovered in my files references indicating that there are many reports in the literature suggesting endocrine bases for epilepsy, as for example, the statements in Cushing's book "Disorders of the Pituitary Body" already quoted on page 100.

Naturally, I began to tell physicians, somewhat timidly at first I admit, that there were possibilities in this organotherapeutic formula in the treatment of epilepsy, especially in children and still more especially in developmentally deficient children where there were other obvious endocrine disorders. Some of them took me at my word and tried the formula clinically with enough success to encourage both them and me, until now I could cite a hundred cases or more in which Antero-Pituitary Co. (Harrower) has been used successfully as a remedy in epilepsy, and, too, not altogether in children that were developmentally defective and had obvious endocrine disorders.

This is empirical, it is true—or was!—and it is rational empiricism I believe, as do hundreds of physicians and parents who have been concerned in problems of this character that have been solved partially or completely by recourse to this "unscientific method".

At this point it may be proper as well as interesting to report an experience I had at the last meeting of the California State Medical Society as published shortly after in *The Organotherapeutic Review* for July 1921.

A well delivered and splendidly illustrated talk had been given by Dr. John L. Tierney, of St. Louis, entitled "Diagnostic Signs of Ductless Gland Disorders." In the course of his remarks he mentioned a number of cases treated by one

form of organotherapy or another, and one of them in particular, illustrated on the screen, was treated with pituitary therapy and later with thyroid therapy—in each instance with unsatisfactory results—and, finally, according to the speaker, a combined therapy accomplished what had been desired. When this statement was made a physician sitting next to me in the dark nudged me very strenuously, and said, “Why in thunder didn’t he start in with pluriglandular therapy?” And so in the lobby of the Hotel del Coronado, immediately following this meeting, I had an interesting discussion with a certain internist about his views of mono- and pluriglandular therapy, and he said to me, and a little crowd of others, in substance:

“In our work we are attempting to get exact information. We treat a given case with the most obviously needed glandular extract. If we fail then, we try another, and so on. If we should give a mixture of these, as you are advising, we would not know which endocrine factor was the most important, or which part of the remedy was doing the work.”

I promptly said that I was perfectly willing to forego this exact information if it involved either failure or temporary failure, and consequent expensive, and perhaps painful, delay to the patient. While new knowledge is to be sought with avidity, and while progress is ever so desirable, the pa-

tient's interests always must come first. "Medicine is the patient and his care; not his disease and its study"—and I believe that it is wrong to spend long periods (for organotherapy involves months and months of treatment) in getting technical information by the patient's response or lack of response to first one form of treatment and then another, and then still another.

The business of a doctor is to cure his patients as quickly and as satisfactorily and as cheaply as possible. If he wants to use them as means to diagnostic ends, then he should treat them for nothing and tell them so at the beginning. It is wrong to take a patient with a pluriglandular dystrophy—and one really can not have a monoglandular dystrophy—and give him a single extract for a while, say a couple of months, then when it doesn't do the work as one might wish, give him another for another couple of months, and so on until the patient either has lost confidence in your organotherapy, or has gone to some other doctor. Frankly, I am astonished at some of the excuses for monoglandular therapy. They may be "scientific", but they are hardly fair to the patient!

One of the organotherapeutic measures that has interested me very much is the use of various glandular desiccations for their galactagogue effect. It happens that desiccated placenta substance contains a certain hormone-like principle

which clinical experience has proved to favor milk production. Now placenta substance is not in the U. S. P., and is ignored by so-called "authorities." For instance, a galactagogue formula containing placenta substance — Placento-Mammary Co. (Harrower)—with several other pluriglandular preparations, was denied admission to the list of New and Non-Official Remedies (*Journal A. M. A.*, January 18, 1919, lxxii, p. 213) because

"Each of the mixtures contains one ingredient or more, which is neither recognized in the U. S. Pharmacopeia nor admitted to New and Nonofficial Remedies, namely: 'Spermin Extract' . . . 'Desiccated Placenta', 'Liver Parenchyma', . . . 'Pancreas Substance' . . . For obvious reasons the Council does not accept a mixture containing an indefinite ingredient and hence it would be necessary as a preliminary for the consideration of any one of the mixtures that their unofficial ingredients be made eligible for New and Nonofficial Remedies by the submission of evidence that such ingredient is of uniform composition and that it is therapeutically valuable when given by mouth. There is no evidence that many of these organs have any value whatever when administered by the mouth or in any other way."

Now it happens that opportunities for applying the principle of "properly supervised controls" can be very conveniently established with the use of a preparation of this character. This has been done with placenta substance and there are a number of reports in the literature indicating that a

certain number of nursing mothers were treated with this form of organotherapy and compared with a certain similar number of apparently similar cases that were treated in the usual manner in different wards of a maternity hospital. The clinical impressions were backed up by figures gained from a study of the amount of milk, its chemical quality and, especially, the weight curve of the infants. These figures proved beyond a peradventure that this particular form of unofficial organotherapy can stand the test of "properly supervised controls". This is not the place to give extensive consideration to reports that prove my remarks but I will give one or two brief items:

In the *Journal A.M.A.* (Dec. 1918, lxxi, p.1861) there is an abstract of an article published originally in *Surgery, Gynecology and Obstetrics* (Nov. 1918, xxvii, p. 535) which has a bearing upon the matter under discussion:

"E. L. Cornell of Chicago reports some experiences with placental extract as a galactagogue. He is decidedly in favor of this measure and backs up his opinion with quite a number of figures. He reports that 87 per cent. of the infants whose mothers received this form of galactagogue treatment began to gain on the fourth or fifth days, as against 69 per cent. of those whose mothers did not take the extract. Of the former class (the treated ones) 44 per cent. regained their birth weight before leaving the hospital against 24 per cent. of the latter."

Again Bertha Van Hoosen, also of Chicago (*Illinois Medical Journal*, Jan. 1920, xxxvii, p. 22), continues a previously published report on the value of placental feeding as a means of stimulating milk production. In this more recent article she gives tables of 33 cases in which placental extract was administered before delivery, and of 36 in which none of this treatment was given. In the first series the babies began to gain at an earlier date and a larger percentage regained their birth weight about the tenth to the fourteenth day as compared with the infants of those mothers who were not treated in this manner.

The point that I want to make, and that I think is perfectly justified, concerns the criticism that the development of organotherapy has not stood the test of "properly supervised controls," and that the practising physician is misled when his attention is directed to the clinical experiences of "ordinary physicians". The greatest progress in medicine has come from the experiences of the "ordinary" doctors. Clinical experiences with the posterior pituitary principle have been of very great value to medicine and through it to humanity, but its clinical value was developed in practice by a gynecologist, W. Blair Bell of Liverpool. Although it is obvious that the utero-tonic influence of this pituitary principle has a clinical reaction that can be and is routinely tested in experimental work, and quite dissimilar from the sug-

gestion recently made regarding the possibility of organotherapy in epilepsy.

The physician who is confronted with a clinical problem must not be denied the opportunity to serve his patient to the utmost no matter whether the physician is going to have an opportunity to check up the results in a "proper" clinical manner with suitable controls, or not. He has no patients that are clinically and physiologically similar to serve as controls to the one to whom he intends to apply a certain measure; and to my way of thinking even if he had the opportunity it would be wrong if one patient is given the benefit of a certain measure and another is denied it in order that the latter may serve as a control so as to further the physician's knowledge. In other words, the strictest application of the principle of "properly supervised controls" in clinical practice means depriving certain individuals of a prospectively helpful measure while using them as control cases for the benefit of the profession.

To revert for a moment to the problem of endocrine epilepsy: If I have two girls under my care whose epilepsy originated in connection with a difficult puberty and whose attacks gave hints of an ovarian origin, I certainly would not feel justified in offering one of the girls Thyro-Ovarian Co. (Harrower) in the hope of modifying the underlying dysovarism presumed to be present, and to deny this same treatment to the other

case and let her get along as best she could on bromides and other sedatives so that I could make suitable comparisons. To my mind, this is reprehensible, for it has been proved times without number that pluriglandular therapy in the type just mentioned *also has a diagnostic value*. This means that the treatment is given not merely with the hope that there may be a salutary modification of the underlying trouble, but that we may learn so much the more regarding the responsiveness of this individual to such stimuli. Thus we develop a few additional hints regarding the possibilities of an endocrine etiologic factor from the clinical response to the organotherapy which is given as much for the diagnostic value as for the therapeutic results.

Surely under such circumstances there is an aspect to the idea of "properly supervised controls" that is not even humanitarian and I have been encouraged in this view many times by the clinical results that have followed; and I believe that these results were not brought about by coincidence or as one man jocularly put it "by a favorable conjunction of the planets."

The general practitioner is not in a position to follow out the routine demanded in great scientific institutions, and I believe that it is impossible for him to expect to develop in his own work a system whereby he can control his clinical results properly. He has to take things as they happen and

are referred to him, and his impressions of the value of therapeutic measures are built upon the constant reiteration of statements by patients which have a similar ring and the repeated discovery of clinical findings which simulate one another.

In other words, if a physician can be led to believe that a certain form of pluriglandular therapy is valuable as a galactagogue he must depend upon what the mothers tell him and upon the resultant findings; and, when these things are proved to his satisfaction, he will use such a remedy routinely irrespective of the comments of the critics and regardless of its failure in some instances, as it is undoubtedly bound to do occasionally.

XI

"THE CRUCIBLE OF THE CLINIC"

"Nothing in medicine is worth more than its yield in practice. Laboratory data and theories as applied to medicine must take the crucible of the clinic where truth and falsehood are separated."—G. W. Crile.

No doubt the reader will have noticed that through all the articles which have been quoted here there runs a similar and characteristic thread—each and every writer uses mild or trenchant words expressing a hope that no longer will the profession have faith in certain clinical findings. He will also notice in several instances that statements previously made have been contradicted; but what is most obvious in the articles is the indubitable fact that all are directed against one individual, and that individual's unswerving attitude.

Just why this concerted action against me should obtain, is beyond my comprehension and would indeed be flattering (I am thinking now that anyone who receives the attention I have received should feel flattered!) were it not that so many misstatements have been made. Am I too sensitive? Am I too willing to believe that the attacks have been directed against me? Let me assume that my opinion was born of outraged feelings that had no foundation in fact, that I took unto myself too much "honor." How then is

the following article to be explained, which appeared in the department "Current Comment" of *The Journal of the American Medical Association* for Nov. 5, 1921, and in which the editor refers to me quite specifically (he admitted to me personally that I was the object of the complimentary (?) remarks) in the following terms:

"This gratuitous postal-card advice to physicians is reenforced by reference to 'monographs' and a trade journal in which scientific medicine is systematically belittled as unpractical. Stripped of their pseudoscientific protective coloration, the 'suggestions' are essentially pleas for gross commercial empiricism. The advertising campaign is ostensibly under the direction of the enterprising Mr. Hyde, the merchant of the firm. Mr. Hyde is a profound admirer of the eminent Dr. Jekyll, the medical director. Dr. Jekyll's principles of physiology are constantly extolled though professional physiologists remain in ignorance of them. Dr. Jekyll, the pathologist, is cited as one speaking with authority, though one seeks in vain his name in the accepted literature of pathology. Dr. Jekyll, the pharmacologist and therapist, is much to the fore, though his work so far fails to appear in the reliable monographs and textbooks on these subjects. Reciprocating, Dr. Jekyll misses no opportunity to say a favorable word for the commercial products of Mr. Hyde. Unfortunately, the relation of endocrinology to sound therapeutics is still largely undetermined. The obligation that rests on competent therapeutic specialists to further work in this field is obvious. But until the truth is deter-

mined, common honesty as well as prudence demands circumspect discrimination."

This criticism is the sort that is thrown off by a greatly prejudiced person who refuses stubbornly to see any good in something that is not to his liking. Moreover, it is unfair because it is divorced from truth; it is unfair because it purposely hides facts; it is unfair because it assumes a superior attitude toward me for the reason that I am not telling the truth, when the article itself states clearly that the truth is not yet determined!

I am told that I am "consistently trying to belittle scientific medicine." This is a wrong conception of my "gesture" toward scientific medicine, for my motives always have been to further its cause, not by methods which a small coterie may think the only proper methods, but by those which rest on a broad basis and necessarily must appeal to broad-minded men.

When taken to task by me about all this in his office in Chicago, in the hour between 11 A. M. and 12 M., Monday, March 13, 1922, Dr. Simmons, titular editor of the *Journal A. M. A.*, stated in substance:

That I was indeed the one referred to in the offensive editorial, even though my name was not mentioned;

That I should not set myself up as a physician and manufacture remedies as well—it was unethical;

That I was "not a scalawag," but that my statements, if not actually dishonest, were too enthusiastic and, consequently misleading;

That I was building far too great a superstructure upon a very flimsy foundation which would very soon fall to the ground, and bring me and many members of the A. M. A. who believe in me down into disrepute;

That at a recent meeting in Baltimore it was decided that my work was detrimental to the best interests of real scientific medicine (or words to that effect);

That the editorial was not written in the house but was submitted from without, and

That there was not malicious intent, libel or whatever it might have been considered by some to be.

I spent the rest of that hour assuring Drs. Simmons and Fishbein that I had as much right to my opinions as they or my critics in Baltimore, that I absolutely believed I was in the right, and that not a single line of the criticism either in the editorials or the original articles was constructive—they are not offering something better; and that negative criticism was exactly in line with what has been meted out to others who happened to be a bit ahead of the times and of others who were not sure of themselves.

And until some really constructive criticism is available and my results to date can be shown to

be unreal, I shall keep on—what else could I do?—and shall expect those who are not biased and who think for themselves, to remain on my side.

The information in the foregoing chapters has been collated largely to show that certain physiologists evidently are not capable of passing ultimate judgment upon therapeutic procedures and that the best intentioned of them are liable to err, both in judgment and in their statements.

To become proficient in the practice of medicine it is necessary to practice medicine. Useful information should not be discarded just because it is not popular with some physicians; it should be acquired *and put to the test*. When a physician is thus fortified he is in a position to defy criticism and be strengthened in a knowledge that is fuller than it had been. He can look the whole world in the face, and not falter. His convictions are his strength; his misgivings would be his weakness. And it is only through convictions that he arrives on a higher plane—a plane that gives him hope that he is not altogether in the wrong.

In concluding this book of "adventures" I would like to leave an impression which I gained some time ago by reading some lengthy correspondence in the *Journal A. M. A.* during the year 1916 between certain physicians and physiologists regarding an important aspect of the internal secretions first emphasized by Dr. G. W. Crile, of Cleveland, Ohio.

Doctor Crile delivered an epoch-making address before the New York Academy of Medicine entitled "The Kinetic Drive," which was published in the *Journal A. M. A.* for December 18, 1915, lxx, p. 2129. Later he was taken to task regarding some physiological aspects of his opinions in a long communication by A. J. Carlson, a physiologist, by the way, and not a physician, who hinted at "forced assumptions and misapplications of experimental data necessary to explain the modus of the kinetic drive." Crile's reply was published simultaneously and my recollection of his last paragraph has prompted me to look up this matter in order to be able to quote his excellent conclusions. After giving several additional reasons for his deductions and defending his position, Crile writes:

"In closing, I may repeat that nothing in medicine is worth more than its yield in practice; that laboratory data and theories as applied to medicine must take the crucible of the clinic where truth and falsehood are separated. The kinetic theory has been tried on a large scale. Up to the present time, in my clinic, the kinetic theory has proved true, as is evidenced (a) by the prevention and control of surgical shock; (b) by the treatment of peritonitis or other infections; (c) by the interpretation and increased control of acidosis and (d) by the operative and non-operative control of exophthalmic goitre and in general, the course of more than ten thousand surgical cases. The kinetic theory harmonizes the phenomena of

many diseases and relates them to physical chemistry rather than to physiology."

Are a clinician's words of so little value that they should be entirely neglected? Is his experience based on hundreds of cases of no value? How about the physiologist without this experience? Are his words golden while the clinician's are pinchbeck? The physiologist has an important rôle to play—a very important one. But by admitting this, I am not at all convinced that his dicta are always tenable. Guinea-pigs and rabbits inside the laboratory have become gods to the laboratory worker, but to the clinician they are often little tin gods on wheels. And, I think, rightly so.

I am modest enough to admit that I am not the equal of Dr. Crile and that I should resent anyone pushing me forward into a position similar to the one which he occupies today in the medical world. But there is something about my own experience which reminds me of Dr. Crile's difficulties some years ago, which took the form of attacks on his opinions and reputation quite similar to those criticisms that are being meted out to me today.

"The crucible of the clinic," as Dr. Crile says, is the place where the real and useful are separated from the false and ephemeral. This sort of crucible is quite to my liking and also to my way of thinking, hence it is just the sort of test to

which I am willing to subject my "medical philosophy" and my products. On the other hand, I would be loath to abide altogether by what issues from the physiologist's laboratory, since I am convinced that clinical experience is the most enlightening experience that the medical man can have.

Let me add that it was necessary in writing this book to make all statements personal, for which unusual act I hereby ask the reader's kind indulgence. The personal note in all books is to be deprecated when it is not absolutely necessary, but, as just intimated, in this instance it could not be avoided. References and quotations were just as necessary, but here no apology is needed. They are component parts of books which lack the personal note.

Another matter which should be mentioned here concerns my object in writing this book. No doubt I shall be criticised by some; no doubt I shall be praised by others. This is the fate of all men who put their thoughts on paper. But I believe that it is wrong to repress one's innermost thoughts, especially when these demand some form of expression; and though I cannot agree with him who thinks it wise always to rush into print, I certainly cannot agree with him who thinks that silence is always the best policy. Hence my object in writing this book is not a bid

for fame, or as my detractors no doubt will put it, for notoriety, but to place before all unbiased readers the trials and tribulations of a "commercial" endocrinologist.

APPENDIX

Several persons, all of them disinterested, some of them with no previous knowledge of this controversy, and at least one of them a non-medical man, have read the manuscript for this book. There seems to be quite a unanimity of opinion that I have not defended myself as thoroughly as possible in regard to the criticized *commercial aspects* of my work.

Of course it is very evident that the "big noise" that I have been making has contributed largely to this ruffled state of mind on the part of the men whom I have taken to task, for every one of them has heard or even seen, on this hand and on that, evidences of our progress.

The editorial writer in *The Journal of the American Medical Association*, it will be remembered, in his editorial "Endocrinology and Pseudoendocrinology" (*J. A. M. A.*, November 5, 1921, lxxvii, p. 1499) stated that—

"Those who purpose acting as purveyors to the medical profession must accept the status of purveyors. The only legitimate means by which they properly can aspire to success are skill in production and acumen in marketing. Equally well established is the principle that the physician or laboratory investigator in the medical sciences shall not exploit for commercial gain the results of his studies."

The same impression was gained from the lecture of Doctor MacCallum and just as I have

stated already, I can only reiterate here that the work that I had hoped might be done by others and which I found would have to be done by myself, could only be financed by the establishment of a business *on a profitable basis*. We have done this in spite of early assurances regarding its soon and certain failure, and hence the criticism.

Now, I have yet to find a physician who is entirely disinterested in matters concerning "profit." Doctor Simmons himself receives a good salary and some of the best men in medicine today are those who have the facilities for developing information and surrounding themselves with a halo of progress, thus making themselves more obvious to their colleagues and, invariably, to their bankers.

Medicine assuredly is a science, but all those who practice it must realize that it is just as much a business, and I disagree with those who say that a man cannot be a physician and at the same time "exploit for gain the results of his studies". Doctor E. R. Squibb, of New York, was an honorable physician and his memory is still respected highly. He went into the drug manufacturing business and remained a physician, and his medical identity has never been submerged from that day to this. Doctor Wallace C. Abbott, of Chicago, with whom I had the honor to be associated for some years, was first, last and all the time a physician, and he developed a manufacturing business

of very respectable proportions. While he had to put up with a good deal of ignominy from the very sources where I have encountered it, he forged ahead and has left a monument to his illustrious memory—The Abbott Laboratories.

Doctor G. H. Sherman, of Detroit, a man who has done more than any other single physician to develop bacterial vaccine therapy in this country and who, I understand, has quite the largest business in this line in the United States, was a physician, and still is. When I was in Detroit a while ago, the president of the Wayne County Medical Society was an employee of the scientific department of Parke, Davis & Co. There is plenty of precedent for me to follow.

I recall a little incident that happened at the State Medical Society meeting held in the Hotel Ambassador in Santa Barbara two or three years ago. A friend of mine was talking with a certain laboratory worker from Los Angeles. Not having seen this friend for some months I went up to him and shook hands and learned that his interest in my work was growing and heard some nice things about it. The laboratory worker, on the other hand, expressed disdain, and in the course of his remarks said that "Harrower is an advertiser." I promptly defended myself and said that it wasn't fair to make such a comparison, because when the word "advertiser" is applied to a physician, ordinarily it means a phy-

sician who believes in newspaper and other trade methods of publicity—"an advertising doctor," or, as some have it, "a quack doctor".

I was not then and am not now doing anything of the kind and I do not expect to, for my advertising is limited to the medical profession and we have no dealings whatever with the laity, save only at the request of interested physicians.

My friend then gave the laboratorian a good jolt by asking him first if he had a paper on the program, and on receiving an affirmative answer asked, "And what is the idea of your coming to this meeting? Aren't you an advertiser? Are you not interested in securing as much referred work as possible from those who may be interested by your remarks? And, really, isn't the whole proposition of State medical meetings, incidentally, a splendid advertising scheme for those who manage to get their names on the program so routinely each year?" And then he finished by saying, "Shame on you! You're as bad an advertiser as Harrower!"

Now I am not saying whether my friend was entirely right or not, but I do know that this laboratory worker, and Doctor Simmons, and Doctor MacCallum, and Doctor Frank, and any others who oppose are absolutely wrong when they question my right to do as I have done.

We have built up an effective, honest, business organization. We have built it upon the ground

principles of *service to the profession*, the very best kind of products possible, and then more service to the profession. In fact, the slogan which I started with and which I adhere to most conscientiously, is "*At YOUR Service*,"—see it below—and just because in the course of my work it is necessary on sound business principles to arrange for a reasonable profit in return for the effort, is this especially worse than to charge \$100 or \$500 or \$1,000 for an operation? or, for that matter any kind of a fee for any kind of medical service?



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